

A Study of Role of Immunohistochemical Markers in Management of Carcinoma Breast

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Abstract:

Background: Breast carcinoma remains the most commonly diagnosed malignancy among women worldwide and a leading cause of cancer-related mortality. Immunohistochemical (IHC) markers such as estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 (HER2/neu) provide crucial prognostic and predictive information, enabling personalized treatment strategies. Differences in receptor expression according to menopausal status may influence disease behaviour and therapeutic outcomes.

Aim and Objectives: To evaluate the expression of ER, PR, and HER2/neu in breast carcinoma and assess their association with menopausal status. The study also aimed to compare receptor expression patterns between premenopausal and postmenopausal women and determine their utility in guiding prognosis and treatment.

Methodology: This prospective observational study was conducted over 22 months in the Department of General Surgery, Government General Hospital, Guntur. Sixty women with histologically confirmed breast carcinoma were enrolled and categorized into premenopausal (n=30) and postmenopausal (n=30) groups. Clinical, demographic, pathological, and reproductive data were collected using a structured proforma. Immunohistochemical analysis for ER, PR, and HER2/neu expression was performed using standardized protocols, and comparative statistical analysis was undertaken.

Results: The mean age was significantly lower in premenopausal women (42.8±3.4 years) than postmenopausal women (62.1±7.6 years; p<0.001). Invasive ductal carcinoma was the predominant histological subtype in both groups (90%). ER positivity was observed in 36.7% of premenopausal and 53.3% of postmenopausal patients, while PR positivity was noted in 33.3% and 50%, respectively. HER2/neu positivity was significantly higher among premenopausal women (43.3% vs. 20%; p=0.05). Triple-negative breast cancer was identified in 20% of premenopausal and 23.3% of postmenopausal patients. Hormonal therapy eligibility was higher among postmenopausal women (50% vs. 33.3%).

Conclusion: Postmenopausal women demonstrated higher ER and PR expression, indicating greater responsiveness to endocrine therapy, whereas premenopausal women exhibited increased HER2/neu positivity, suggesting more aggressive tumor biology. Routine assessment of IHC markers is essential for prognostication and individualized management of breast carcinoma.

Keywords: Breast Carcinoma, Immunohistochemistry, Estrogen Receptor, HER2/neu, Menopausal Status.

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Introduction

Breast carcinoma continues to be the most commonly diagnosed malignancy and one of the leading causes of cancer-related mortality in women globally. Despite advances in screening and early detection, the disease burden remains significant, particularly in developing countries. Early diagnosis and appropriate management are essential to improve patient survival and quality of life. Traditionally, clinical and histopathological parameters such as tumor size, histological grade, and axillary

lymph node status have been utilized as key prognostic factors to guide treatment decisions in breast cancer. [1] However, recent developments in molecular biology have led to a paradigm shift in the approach to breast cancer diagnosis and treatment. Increasing emphasis is being placed on the evaluation of biological molecular markers that offer both prognostic and predictive information. This shift is warranted due to the recognition that a considerable number of patients with early-stage breast cancer

may already harbor microscopic metastatic disease at the time of diagnosis, which may not be detected through conventional histopathological means. [2,3] The immunohistochemical expression of hormone receptors such as estrogen receptor (ER) and progesterone receptor (PR), along with the human epidermal growth factor receptor 2 (HER2/neu), has become a critical component of breast cancer profiling. These markers help stratify patients into subgroups that respond differently to hormonal therapy and chemotherapy. The presence or absence of these receptors not only influences prognosis but also determines therapeutic strategies, thereby personalizing patient management. [4]

The present study aims to explore the pattern of immunohistochemical marker expression in breast carcinoma and to evaluate the differences in expression between premenopausal and postmenopausal women. Understanding these differences could assist in tailoring treatment strategies more effectively and contribute to the overall improvement of breast cancer outcomes.

Aims: To study the expression of key immunohistochemical markers—ER, PR, and HER2/neu—in breast carcinoma and to assess their association with menopausal status.

Objectives: To evaluate the expression of immunohistochemical markers in patients diagnosed with carcinoma breast. To compare the expression patterns of ER, PR, and HER2/neu among premenopausal and postmenopausal women. To determine the prognostic significance of these markers in the context of menopausal status. To assess the utility of these markers in guiding further therapeutic management in a tertiary care setting.

Methodology

This was a hospital-based, prospective observational study done in the Department of General Surgery, Government General Hospital, Guntur, a tertiary care teaching hospital affiliated with Dr. NTR University of Health Sciences over a period of 22

months, commencing from the date of ethical approval granted by the Institutional Ethics Committee.

A total of 60 female patients diagnosed with carcinoma breast were enrolled in the study. The participants were categorized into two groups: Group A: 30 consecutive premenopausal women. Group B: 30 consecutive postmenopausal women.

Inclusion Criteria: Female patients aged between 30 and 70 years. Histologically confirmed diagnosis of carcinoma breast. Patients who provided informed written consent to participate in the study.

Exclusion Criteria: Patients younger than 12 years or older than 70 years. Patients with distant metastasis or recurrent carcinoma breast. Individuals with prior history of hysterectomy or other malignancies. Male breast cancer patients. Patients unwilling to undergo necessary investigations or treatment. Patients diagnosed with advanced carcinoma not amenable to curative treatment.

Data Collection and Analysis: Clinical and pathological data were collected using a structured proforma. Immunohistochemical analysis of ER, PR, and HER2/neu expression was carried out as per standardized protocols. The findings were documented and analyzed using appropriate statistical methods. Comparative analysis was conducted between the two groups, and the results were interpreted in the context of existing literature.

Ethical Considerations: Informed consent was obtained from all participants for interviews, examinations, and storage of clinical images. Patient confidentiality and data protection were strictly maintained throughout the study. The study adhered to the principles of the Declaration of Helsinki. Participants were informed of their right to withdraw from the study at any point without any impact on their standard care. No animal or invasive experimental procedures were involved in the study.

Results

Table 1: Demographic Profile Comparison

Parameter	Premenopausal (n=30)	Postmenopausal (n=30)	p- value
Mean Age (years)	42.8 ± 3.4	62.1 ± 7.6	<0.001
Early Menarche (<12 yrs)	24 (80%)	10 (33%)	<0.001
Mean Age at 1 st Pregnancy	27.1 ± 4.3	23.8 ± 3.1	0.001

Table 2: Reproductive History and Family History

Parameter	Premenopausal (n=30)	Postmenopausal (n=30)	p- value
Multiparity	25 (83.3%)	27 (90%)	0.240
Breast feeding ≥12 months	8 (26.7%)	21 (70%)	0.005
Family History of Ca Breast	2 (6.7%)	0	0.079

Table 3: Clinical Features

Symptom	Premenopausal (n=30)	Postmenopausal (n=30)	p-value
Lump	30 (100%)	30 (100%)	-
Pain	2 (6.7%)	1 (3.3%)	0.55
Skin Changes	1 (3.3%)	5 (16.7%)	0.05
Nipple Retraction	2 (6.7%)	3 (10%)	0.40
Nipple Discharge	0	2 (6.7%)	0.15
Mean Duration (wks)	8.7	10.5	0.06

Table 4: Tumor Size and Clinical Stage

Tumor Size	Premenopausal	Postmenopausal	Total
≤2 cm	6	3	9
>2–<5 cm	21	23	44
>5 cm	3	4	7
Stage IA	1	0	1
Stage IIA	6	8	14
Stage IIB	10	8	18
Stage IIIA	6	8	14
Stage IIIB	7	6	13

Table 5: Histopathological Subtypes

Histological Type	Premenopausal	Postmenopausal
Invasive Ductal Carcinoma	27	28
IDC + Medullary	1	0
IDC + Mucinous	1	0
IDC + Intraductal Papillary	0	1
Papillary Carcinoma	0	1

Table 6: Receptor Expression

Marker	Status	Premenopausal	Postmenopausal	p-value
Estrogen	Positive	11 (36.7%)	16 (53.3%)	0.22
Progesterone	Positive	10 (33.3%)	15 (50%)	0.15
HER2/neu	Positive	13 (43.3%)	6 (20%)	0.05
Triple Negative	Yes	6 (20%)	7 (23.3%)	NS

Table 7: Treatment Profile and Outcomes

Treatment Type	Premenopausal	Postmenopausal	p-value
Mastectomy	26	25	NS
Breast Conserving	4	5	NS
Chemotherapy	28 (93.3%)	24 (80%)	0.027
Radiotherapy	5 (16.7%)	4 (13.3%)	NS
Recurrence	1 (3.3%)	2 (6.7%)	NS

Table 8: Tumor Quadrant Involvement

Tumor Quadrant	Premenopausal (n=30)	Postmenopausal (n=30)
Upper Outer	20 (66.7%)	22 (73.3%)
Central	7 (23.3%)	5 (16.7%)
Upper Inner	2 (6.7%)	2 (6.7%)
Lower Quadrants	1 (3.3%)	1 (3.3%)

Laterality of Tumor (Unilateral vs. Bilateral): All patients in this study presented with unilateral breast involvement. No cases of bilateral breast cancer were observed in either group. While bilateral breast cancer is less common, it is often associated with genetic predispositions such as BRCA mutations. The absence of bilateral cases in this cohort may reflect the non-hereditary nature of

most breast cancers in the study population. Skin and Nipple Involvement: Skin changes such as peau d'orange and ulceration were reported more frequently in postmenopausal women (16.7%) than in premenopausal women (3.3%). This may be attributed to delayed presentation or more advanced local disease in the elderly population. Nipple involvement, including retraction and discharge, was

observed in both groups. Although not statistically significant, nipple retraction was noted slightly more often in postmenopausal women (10%) versus premenopausal (6.7%), while nipple discharge was absent in premenopausal women and present in 2 postmenopausal cases. These findings are crucial, as nipple and skin changes can indicate more advanced disease, including involvement of subareolar ducts and skin infiltration.

Hormonal Therapy Eligibility: Hormonal therapy, particularly with selective estrogen receptor modulators (SERMs) or aromatase inhibitors, is a cornerstone in the treatment of hormone receptor-positive breast cancer. In this study, patients eligible for hormonal therapy were identified based on ER and/or PR receptor positivity. A total of: 10 (33.3%) premenopausal and 15 (50%) postmenopausal women were hormone receptor-positive and thus eligible for endocrine therapy. This higher proportion in the postmenopausal group is consistent with literature indicating increased hormone sensitivity of breast tumors in older women.

Triple Negative Breast Cancer (TNBC): Triple-negative breast cancer, defined by the absence of ER, PR, and HER2 expression, is known for its

aggressive behavior and limited treatment options due to the lack of targeted hormonal or HER2-directed therapies. In this study: 6 (20%) premenopausal and 7 (23.3%) postmenopausal patients were diagnosed with TNBC. Although slightly more prevalent in postmenopausal women, the difference was not statistically significant. TNBC patients in both groups were treated with chemotherapy as the primary systemic modality. Follow-up data showed no immediate recurrence within the one-year observation period for these patients.

Histological Grade: While the majority of tumors were classified histologically as invasive ductal carcinoma (IDC), further grading into Grade I, II, or III tumors based on cellular differentiation was done. It was observed that: Grade II and III tumors were more frequent among premenopausal women, suggesting a tendency toward more aggressive tumor biology in the younger age group. Postmenopausal women had a slightly higher proportion of well-differentiated (Grade I) tumors.

These differences, though not statistically significant in this cohort, are clinically important as histological grade correlates with tumor aggressiveness and prognosis.

Table 9: Hormonal Therapy Eligibility

Group	ER/PR Positive Patients	Eligible for Hormonal Therapy
Premenopausal	10 (33.3%)	Yes
Postmenopausal	15 (50%)	Yes

Discussion:

Table 10: Demographic Profile

Study	Premenopausal	Postmenopausal	Remarks
Present Study	42.8 ± 3.4	62.1 ± 7.6	Significant difference
Surakasula et al. (2014) [5]	45.0	55.0	Similar pattern
Sandhu et al. (2010) [6]	47.4	56.5	Consistent findings
Ghosh et al. (2011) [7]	49.0	Not specified	Comparable
Raina et al. (2005) [8]	47.0	Not specified	Reinforces trend

Early menarche (<12 years) was more prevalent among premenopausal women, supporting theories related to prolonged hormonal exposure. Additionally, the age at first pregnancy was higher in premenopausal women, an established risk factor for breast cancer.

Table 11: Reproductive History

Study	Breastfeeding ≥12 mo (PreMeno)	Post Meno	Comments
Present Study	26.7%	70%	Statistically significant
Meshram et al. (2009) [9]	Lower duration noted	Not specified	Associated with increased risk
Gajalakshmi et al (2009) [10]	Reduced risk observed	No effect	Protective in premenopausal only
Parikh et al. (2021) [11]	Not specified	Not specified	Association with reproductive factors
Kaur et al. (2011) [12]	Lower duration noted	Not specified	Consistent with Mincreased risk

Family history of breast cancer was noted in 6.7% of premenopausal patients and none in postmenopausal patients, suggesting a sporadic pattern consistent with other studies.

Table 12: Clinical Presentation

Study	Skin Changes (PreMeno)	PostMeno	Notable Findings
Present Study	3.3%	16.7%	Trend toward late diagnosis in elderly
Surakasula et al. (2014) [5]	Late presentation common	Late presentation common	Consistent observation
Sharma et al. (2021) [13]	Not specified	Not specified	Younger age at presentation
Bhatnagar et al. (2019) [14]	Not specified	Not specified	Epidemiological characteristics noted
Bose et al. (2020) [15]	Not specified	Not specified	Large dataset analysis

Table 13: Tumor Characteristics

Study	Tumor Size 2–5cm (PreMeno)	PostMeno	Axillary LN Involvement (PreMeno)	PostMeno
Present Study	53.3%	66.7%	66.7%	66.7%
Kocaöz et al (2019) [16]	Larger tumors noted	Smaller tumors	Higher in Premenopausal group	Lower
Patel et al. (2018) [17]	Not specified	Not specified	Related to tumor characteristics	Related
Das et al. (2017) [18]	Not specified	Not specified	High grade tumors prevalent	Consistent findings
Ahmed et al. (2018) [19]	Not specified	Not specified	High grade tumors and positive nodes	Consistent with present study

Table 14: Histopathological Findings

Study	Invasive Ductal Carcinoma (PreMeno)	PostMeno	Comments
Present Study	90%	90%	Predominant subtype
Kocaöz et al.(2019)16	49.5%	50.5%	Similar distribution
Ahmed et al.(2018)19	88%	85%	Consistent findings
Gupta et al.(2020)20	Not specified	Not specified	Large dataset analysis
Thakur et al. (2019)21	Not specified	Not specified	Clinicopathological features compared

Conclusion

Breast carcinoma remains one of the most common malignancies affecting women worldwide, with varied biological behavior and clinical outcomes based on hormonal and molecular profiles. Immunohistochemical (IHC) evaluation of estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 (HER2/neu) has become indispensable in modern breast cancer diagnostics and management. These markers not only aid in sub classifying breast tumors but also help determine prognosis and tailor individualized treatment regimens.

In this prospective comparative study involving 60 patients—30 premenopausal and 30 postmenopausal women with histologically confirmed carcinoma breast—several important observations were made: The mean age of presentation was significantly different between the two groups, aligning with established age-related patterns of breast cancer incidence. Premenopausal women were more likely to present with higher tumor grades and increased HER2/neu positivity, suggesting a tendency toward more aggressive tumor biology. In contrast,

postmenopausal women showed higher ER and PR positivity, indicating better responsiveness to hormonal therapy and a more favorable prognosis. Triple-negative breast cancers (TNBC), although relatively balanced between the two groups, remain a clinical challenge due to their aggressive nature and limited targeted treatment options. Mastectomy was the predominant surgical choice across both groups, with a greater frequency of chemotherapy administration in premenopausal patients. Hormone receptor-positive patients, particularly in the postmenopausal group, benefited from endocrine therapy, highlighting the clinical utility of IHC profiling in guiding treatment.

The study reinforces the pivotal role of immunohistochemical markers in the comprehensive evaluation of carcinoma breast. The observed variations between premenopausal and postmenopausal patients underscore the biological heterogeneity of the disease and the necessity for stratified treatment approaches. These findings are consistent with global literature and emphasize the importance of integrating molecular diagnostics into routine clinical practice.

Implications for Practice: Routine assessment of ER, PR, and HER2/neu status should be mandated for all breast cancer patients to guide therapeutic decisions effectively. Stratification by menopausal status can help anticipate disease behavior and facilitate more personalized management strategies. Special attention should be given to TNBC subtypes, which necessitate early detection and aggressive multimodal treatment.

Limitations of the Study: The study was limited by a modest sample size and was conducted at a single tertiary care center, which may affect generalizability. Long-term outcomes such as disease-free survival and overall survival could not be assessed within the study duration. Lack of Ki-67 index and genomic profiling are potential gaps that future studies can address. Recommendations for Future Research: Larger, multicenter studies with extended follow-up are needed to validate these findings and assess long-term outcomes. Inclusion of additional biomarkers such as Ki-67, p53, and BRCA mutation analysis could enhance the understanding of tumor biology. Comparative evaluation of therapeutic response and survival rates across menopausal subgroups may provide further insight into optimizing breast cancer management.

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