



Comparison of Receptor Status in Breast Carcinoma Between Premenopausal and Postmenopausal Women

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Abstract: *Background:* Breast cancer is the most prevalent cancer affecting women worldwide. The immunohistochemical status of estrogen receptors (ER), progesterone receptors (PR), and human epidermal growth factor receptor 2 (HER2) plays a crucial role in determining breast cancer treatment options and prognosis. These receptor statuses are known to be influenced by menopausal transition. *Objective:* This cross-sectional comparative study aimed to assess the frequency of ER, PR, and HER2/Neu positivity or negativity and their association with menopausal status among female breast carcinoma patients. *Methodology:* The study was conducted over one year, from September 2021 to August 2022, at the Department of Surgery, Rajshahi Medical College, Rajshahi. A total of 50 female patients with breast carcinoma were included in the study, divided into two groups: Group A (Premenopausal women) and Group B (Postmenopausal women). Specimens were collected after modified radical mastectomy and sent to renowned laboratories for histopathological and immunohistochemical receptor assays. Data were collected through a predesigned semi-structured questionnaire and analyzed using SPSS (version 24.0). *Results:* The study found no significant relationship between receptor status and menopausal status or increasing age. However, a significant histopathological association was observed with receptor status, with ER and PR positivity associated with grade II tumors (p -value <0.011). The most common histopathological type was ductal cell carcinoma, and its incidence increased with parity (p -value <0.009). *Conclusions:* This study revealed no significant difference in hormone receptor and HER2 Neu expression between premenopausal and postmenopausal breast carcinoma patients. Further research with a larger sample size is recommended for a more comprehensive understanding of this relationship.

Keywords: Breast cancer, Hormone receptor, HER2 Neu, Premenopausal, Postmenopausal.

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Article at a glance:

Study Purpose: The study aims to compare the expression of estrogen receptors (ER), progesterone receptors (PR), and human epidermal growth factor receptor 2 (HER2) in premenopausal and postmenopausal women with breast carcinoma in Bangladesh.

Key findings: No significant difference in ER, PR, and HER2 expression between groups. Histopathological grading linked to ER/PR positivity.

Newer findings: The study provides localized data on breast cancer markers in Bangladesh, highlighting the complexity of receptor expression patterns and emphasizing the need for regional-specific information for effective clinical decision-making.

Abbreviations: ER: Estrogen Receptor, PR: Progesterone Receptor, HER2: Human Epidermal Growth Factor Receptor 2, FNAC: Fine Needle Aspiration Cytology, TNBC: Triple Negative Breast Cancer



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INTRODUCTION

Breast cancer is a global health concern, particularly affecting women. While the incidence of breast cancer is lower in developing countries

compared to their Western counterparts, it is on the rise, making it the second leading cause of cancer-related deaths among females.¹ A staggering 62% of breast cancer-related deaths occur in developing

nations. Bangladesh, with a population exceeding 163 million, is among the most densely populated countries globally. The female population outnumbers the male population, with around 45 million women of reproductive age and 13.5 million women aged over 50 years.² Despite this demographic landscape, comprehensive data on breast cancer in Bangladesh remains limited.

The National Institute of Cancer Research and Hospital (NICRH) is the sole institution systematically tracking new cancer cases in the country. According to NICRH reports, between 2005 and 2010, 5255 breast cancer cases were diagnosed, with an average patient age of 41.8 years and over 56% of cases occurring in women of reproductive age (15–44 years).³ Additionally, postmenopausal women in Bangladesh are reported to be 27.83% more likely to develop breast cancer than their premenopausal counterparts.⁴ Numerous international studies have investigated the frequency of ER, PR, and Her-2 Neu positivity in breast cancer and their prognostic and predictive significance. Generally, receptor positivity is inversely correlated with Her-2 Neu expression. ER and PR negativity, along with Her-2 Neu positivity, are associated with higher tumor grade, larger tumor size, increased lymph node involvement, and more aggressive histopathological types.⁵

OBJECTIVES

General objective

- To compare the expression of receptor status between premenopausal and postmenopausal women having breast carcinoma.

Specific objectives

- To assess the ER, PR, and HER 2-receptor status in premenopausal women
- To assess the ER, PR, and HER 2-receptor status in postmenopausal women.
- To assess the relationship between histopathological grading and receptor status in breast cancer.
- To assess the relationship of histological type with receptor status in breast cancer.

MATERIALS AND METHODS

Study Design

This study employed a cross-sectional comparative design and was conducted over 12

months from September 2021 to August 2022. The research was conducted at the Department of Surgery, Rajshahi Medical College, Rajshahi, Bangladesh. The study included a total of 50 female patients diagnosed with breast carcinoma.

Inclusion Criteria

- Female patients diagnosed with breast carcinoma.
- Both premenopausal and postmenopausal women are eligible for inclusion.

Exclusion Criteria

- Patients without histologically confirmed malignant breast tumors.
- Patients with a history of recurrent breast carcinoma.
- Patients are currently undergoing neoadjuvant therapy for breast cancer.
- Breast cancer patients diagnosed with concomitant malignancies other than breast cancer.
- Patients who have undergone surgical menopause and do not experience natural menopausal transitions.

Data Collection

A predesigned semi-structured questionnaire collected demographic and clinical data, including age, menopausal status, parity, tumor grade, and histopathological type. Data were collected by trained personnel. Tissue specimens obtained from the participants were sent to two reputable laboratories for histopathological examination and immunohistochemistry to assess the status of estrogen receptors (ER), progesterone receptors (PR), and human epidermal growth factor receptor 2 (Her2 Neu). Histopathological data were collected to determine tumor grade and type.

Data Analysis

By a predesigned semi-structured questionnaire collected demographic and clinical data, including age, menopausal status, parity, tumor grade, and histopathological type. The data analysis was conducted using the Statistical Package for the Social Sciences (SPSS) software, specifically version 24.0.

RESULT

Table 1: Age Distribution of Premenopausal and Postmenopausal Breast Carcinoma Patients (N=50)

Age category	Menstrual status of the respondents		Total
	Group A (n=25)	Group B (n=25)	
	n (%)	n (%)	
25 to 30 years	6 (100.0%)	0 (0.0%)	6
31 to 40 years	16 (100.0%)	0 (0.0%)	16
41 to 50 years	3 (25.0%)	9 (75.0%)	12
51 to 60 years	0 (0.0%)	12 (100.0%)	12
61 to 70 years	0 (0.0%)	4 (100.0%)	4
Age (mean±SD)	35 (± 5.35)	53.96 (± 7.11)	

Table 1 shows the distribution of both premenopausal and postmenopausal respondents according to their age category (N =50). It reveals that among the respondents of breast carcinoma between 41 to 50 years age group, only 25% of them were premenopausal, which was proportionately less (25% vs 75% respectively) than

postmenopausal women. Other respondents were distributed in different proportions in respective natural age categories of menstrual status. Again, The Mean (±SD) age of premenopausal women was 35 (± 5.35) years, and the mean (±SD) age of the postmenopausal women was 53.96 (± 7.11) years.

Table 2: Frequency of Receptor Status in Premenopausal and Postmenopausal Breast Carcinoma Patients

Receptor Type	Group A (Premenopausal)	Group B (Postmenopausal)	P-value
ER Positive	12 (48%)	13 (52%)	0.82
PR Positive	11 (44%)	15 (60%)	0.34
HER2 Positive	8 (32%)	10 (40%)	0.55

The results indicated no statistically significant difference in ER, PR, and HER2 receptor expression between premenopausal and postmenopausal women. The prevalence of ER and PR positivity was slightly higher in the postmenopausal group, but these differences were

not statistically significant. HER2 positivity was also similar across both groups. These findings suggest that menopausal status does not significantly impact the expression of these receptors in breast carcinoma patients in this study population.

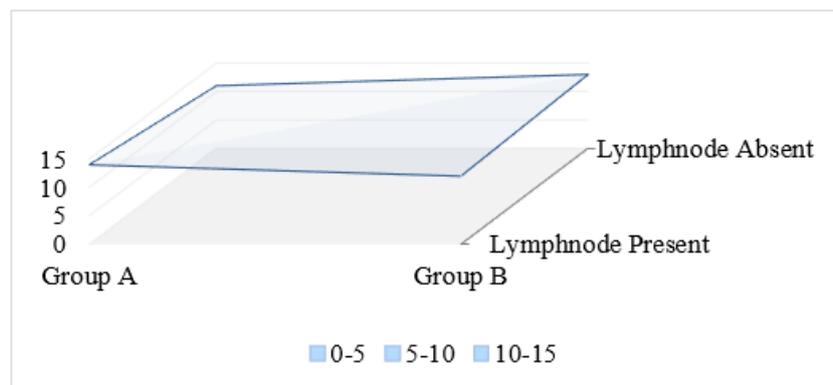


Figure 1: Lymph node involvement status among the respondents with breast carcinoma

Figure 1 shows the relation between menstrual and lymph node involvement status among the respondents with breast carcinoma (N =50). It reveals that more than half (56%) of the premenopausal women had lymph node

involvement, proportionately higher than postmenopausal (Lymph node, premenopausal vs postmenopausal = 56 % vs 48 %) women. The relation between menstrual and lymph node involvement status among the respondents with

breast carcinoma was statistically not significant ($p > .05$).

Table 3: Relationship Between Menstrual Status, Family History, and Parity in Breast Cancer

Parity of Respondents	Premenopausal	Postmenopausal	Total Patients	P-value
Nulliparous	6 (24.0%)	0 (0.0%)	6	<.05s
Parous	19 (76.0%)	25 (100.0%)	44	
Family History of Breast Cancer				
Present	10 (40.0%)	6 (24.0%)	16	>.05ns
Absent	15 (60.0%)	19 (76.0%)	34	

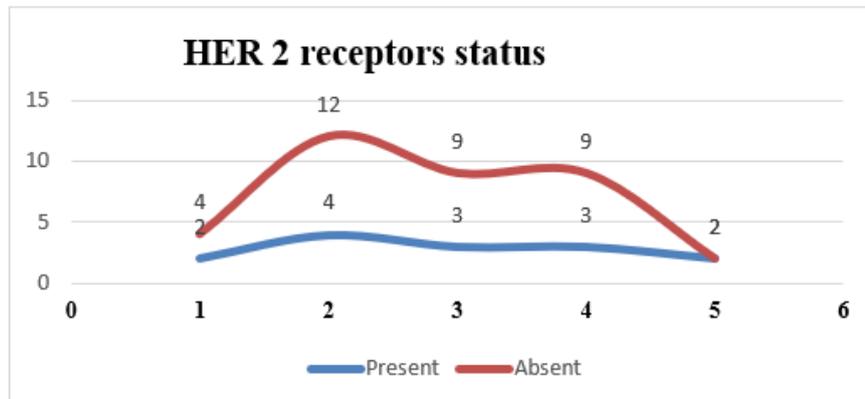


Figure 2: Relation between age category and estrogen and progesterone receptors of breast carcinoma

Figure 2 shows the relation between age category and estrogen & progesterone receptors of breast carcinoma respondents (N =50). It reveals that estrogen and progesterone receptors are more proportionately found in the 61 to 70 years (75%),

25 to 30 years (50%), and 41 to 50 years old age groups (41.7%). The relation between age category and estrogen & progesterone receptors of breast carcinoma respondents was not statistically significant ($p > .05$)

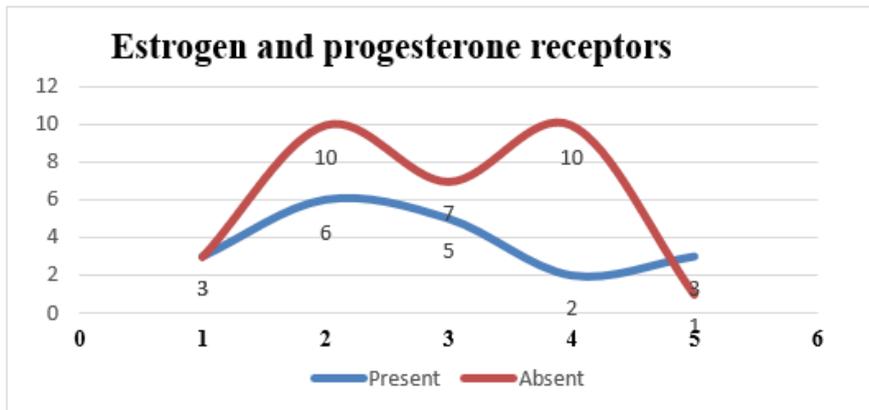


Figure 3 Relation between age category and HER 2 receptors of breast carcinoma

Figure 3 shows the relation between age category and HER 2 receptors of breast carcinoma respondents (N =50). It reveals that HER 2 receptors are more proportionately found in the age groups

between 61 and 70 years (50 %) and 25 to 30 years (33 %) than others. The relation between breast carcinoma respondents' age category and HER 2 receptors was not statistically significant ($p > .05$).

Table 4: Correlation Between Histopathological Grading and Receptor Status in Breast Carcinoma (N=50)

Histopathological Grading	Estrogen and progesterone Receptor Present	Estrogen and progesterone Receptor Absent	HER2 Receptor Present	HER2 Receptor Absent	P-Value
Grade I	3 (100%)	0 (0.0%)	0 (0.0%)	3 (100.0%)	-
Grade II	15 (41.7%)	21 (58.3%)	9 (25%)	27 (75%)	<.05s
Grade III	1 (9.1%)	10 (99.9%)	5 (45.5%)	6 (54.5%)	> .05ns

This table shows the histopathological grading relation with tumor receptor status. It reveals ER & PR are positive mostly in Grade II cancer (41.7%), which is statistically significant (p

value= .011). HER 2 was positive in 25% and 45.5% in Grade I and Grade II, respectively. However, the rest of the relationship is statistically not significant. (p value= >.05).

DISCUSSION

Breast cancer is a multifaceted disease with various molecular and clinical attributes that significantly impact its prognosis and therapeutic approach. In our discussion, we will examine the implications of our study findings about breast cancer markers (ER, PR, HER2), histopathological characteristics, lymph node involvement, age, and menopausal status while also considering the broader context of breast cancer care.

The expression of the HER2 Neu gene and the status of estrogen receptor (ER) and progesterone receptor (PR) are essential in assessing the prognosis and predicting therapeutic outcomes in breast cancer patients. Typically, ER and PR-positive tumors, coupled with HER2 Neu-negative status, are associated with a more favorable prognosis, while the opposite scenario tends to yield a poorer prognosis. These prognostic and predictive indicators are vital in tailoring breast cancer care strategies.⁶

Our study disclosed that the mean age of premenopausal women diagnosed with breast carcinoma was 35 years, whereas postmenopausal women had a mean age of 53.96 years. Consistent with global trends, age remains a pivotal factor in breast cancer risk, with postmenopausal women being at a higher risk due to hormonal changes and increased exposure to estrogen over time. This age discrepancy underscores the importance of considering age in both diagnosis and treatment planning for breast cancer patients.

Ductal cell carcinoma emerged as the most prevalent histological subtype in our study, mirroring the situation in Bangladesh, where approximately 95% of breast cancers are invasive ductal carcinomas.⁷ This finding aligns with international research, which has consistently reported ductal carcinoma as the most common subtype.

Bangladesh has a scarcity of data on breast cancer markers, including ER, PR, and HER2 Neu expression. A retrospective study on 1042 cases in Bangladesh reported ER and PR positivity in 69% and 73% of cases, respectively, and HER2 Neu overexpression in 28% of cases. Triple-negative breast cancer (TNBC) constituted 9% of patients.⁸ These findings broadly align with our study's observations regarding HER2 Neu but differ regarding ER and PR. This discrepancy highlights the need for localized data when making clinical decisions, as the prevalence of these markers can vary across populations.

The correlation between menstrual status and HER2 receptor expression did not yield statistically significant results in our study (p > 0.05). However, a similar study reported significantly higher HER2 positivity in postmenopausal women than premenopausal women. This disparity underscores the complexity of breast cancer and the potential impact of demographic and regional variations on receptor expression.⁹

Our study also explored the relationship between age categories and receptor status.

Estrogen and progesterone receptors were proportionately more prevalent in the 61 to 70 years 25 to 30 years, and 41 to 50 years age groups, although these differences were not statistically significant ($p > 0.05$). Similarly, HER2 receptors were more proportionately found in the 61 to 70 and 25 to 30 age groups, with no significant correlation with age. These findings emphasize the intricate nature of receptor expression patterns in breast carcinoma.

Histopathological grading is a critical determinant of breast cancer prognosis. In our study, grade II carcinoma was the most prevalent grade among both premenopausal (84%) and postmenopausal (60%) women. However, there was no statistically significant relationship between menstrual status and histopathological grading ($p > 0.05$). A similar study observed a much higher incidence (63%) of grade III tumors in Bangladesh, underscoring potential regional variations in histopathological characteristics.¹⁰

In terms of lymph node involvement, our study revealed that more premenopausal women (56%) had lymph node involvement compared to postmenopausal women (48%), though this difference was not statistically significant ($p > 0.05$). Conversely, a similar study found no association between lymph node involvement and menstrual status. These findings suggest that lymph node involvement may be influenced by factors other than menopausal status, such as tumor subtype and stage.¹¹

In our study, estrogen and progesterone receptors were more proportionately present in grade I tumors (100%) than in other grade tumors, with a statistically significant relationship between histopathological grading and estrogen and progesterone receptors ($p < 0.05$). However, HER2 receptors were more proportionately present in grade III tumors (45.5%), with no statistically significant relationship with histopathological grading ($p > 0.05$). These results underscore the importance of considering histopathological grading and receptor status when designing tailored treatment strategies.

While our study did not reveal a significant association between age and receptor status, it is

essential to acknowledge the heterogeneity of breast cancer. Similar studies have reported that young premenopausal women tend to present with higher- grade breast cancer and more negative tumor receptors, highlighting the multifaceted nature of this disease.

CONCLUSION

In this study, no significant differences were observed in the expression of estrogen receptors, progesterone receptors, or HER2 receptors between premenopausal and postmenopausal breast carcinoma patients, with 36% and 40% of each group showing receptor expression. Menstrual status did not correlate with receptor expression, suggesting receptor status is not significantly influenced by menopausal status in this population.

Recommendation

- Conduct extensive studies with larger samples to refine knowledge on hormone receptors in premenopausal and postmenopausal breast cancer patients.
- Increase research funding from public and private sectors, focusing on surgical and related fields.
- Implement detailed regional studies in Bangladesh to explore hormone receptor patterns in breast cancer relative to menstrual status.

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Authors contributions

Dr. Md. Alim Al Razy was the principal investigator, conceiving the study design, overseeing data collection and analysis, and drafting the manuscript. Professor Dr. Md.

Habibullah Sarkar provided critical revisions and intellectual content, ensuring the accuracy and integrity of the work. Asst. Prof. Sheikh Mohd. A. Hakim contributed to the study's conceptualization and methodology development.

Declarations

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