

Original research article

## EVALUATION OF THE PATHOLOGICAL RESPONSE TO NEOADJUVANT CHEMOTHERAPY IN LOCALLY ADVANCED BREAST CANCER

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**Abstract**

**Background and objective:** To assess how patients with locally advanced breast cancer respond pathologically to neoadjuvant therapy. It is uncommon to have locally advanced breast cancer (LABC), and it poses significant clinical challenges. The purpose of the study was to look into the relationship between disease-free survival and the pathological response to neoadjuvant chemotherapy.

**Method:** An observational study was conducted at Department of General Surgery, Deccan College of Medical Sciences, Hyderabad, Telangana, India from December 2022 to November 2023. on a sample of 40 persons to assess the pathological response to neoadjuvant chemotherapy in patients with locally advanced breast cancer. The study received ethical approval from the committee.

**Result:** Between the ages of 50 and 60, 33% of the population fell. About half of the patients exhibited negative human epidermal growth factor receptor 2 (HER2), positive progesterone receptor (PR), and positive oestrogen receptor (ER). Sixty-seven percent of tumours tested positive for both the progesterone receptor (PR) and the oestrogen receptor (ER). Forty percent of the tumours had HER2 positive results. Merely 17% of the patient cohort exhibited a pathological reaction to neoadjuvant chemotherapy (NACT). 83% of the total did not respond.

**Conclusion:** Finding the cancers that are most likely to respond well to specific medications and treatment strategies might significantly improve the prognosis. The most recent developments in our knowledge of cancer biology and genetic analysis can be used to enhance the therapeutic therapy of locally advanced breast cancer (LABC), producing a very effective individualised strategy.

**Keywords:** LABC, NACT, pathological response, breast cancer

**Introduction**

As per the National Cancer Registry Programme, breast cancer accounts for approximately thirty percent of all cancer cases among Indian women, with the largest incidence occurring in metropolitan areas. A broad spectrum of diverse and multifaceted breast cancer types are included in the category of locally progressed breast carcinoma. In affluent nations, it makes up roughly 10–20% of all cases of breast

cancer; but, in India, it makes up over 60% of cases. Varied medical facilities around the world have varied definitions of locally advanced breast cancer. The following are the requirements for inclusion: tumours bigger than five cm that affect the skin or chest wall, regardless of whether regional lymph nodes (N1–N3) are involved. Regardless of the tumor's size, there is involvement of the surrounding lymph nodes. Lymph nodes within the chest wall, lymph nodes above or below the collarbone, and repaired or rearranged axillary lymph nodes [1, 2, 3]. Inflammatory breast cancer used to be considered a subtype of locally advanced breast cancer. The prognosis for inflammatory breast cancer is much poorer than that of noninflammatory forms of locally advanced breast carcinoma. As a result, specific standards were created in order to oversee it [3, 4].

Neoadjuvant therapy is a relatively new treatment modality that has been developed in the last thirty years and is being used worldwide to shrink locally advanced breast cancer that is technically incurable before surgery. Neoadjuvant literally translates as "new treatment added to enhance primary treatment," a term taken from Greek and Latin. In animal models of breast cancer, the observation of accelerated metastatic growth following tumour excision provides the biological rationale for neoadjuvant therapy [5, 6, 7]. With a variable pathologic response rate, neoadjuvant chemotherapy is generally acknowledged as the gold standard for treating locally advanced breast cancer (LABC). The degree of pathological response and long-term results, such as overall survival (OS) and disease-free survival (DFS), are highly correlated. The purpose of this study was to assess how neoadjuvant therapy affected individuals with locally advanced breast cancer in terms of its pathological response [8, 9].

### **Materials and Method**

With the committee's ethical permission, an observational study was conducted at Department of General Surgery, Deccan College of Medical Sciences, Hyderabad, Telangana, India from December 2022 to November 2023. On 40 participants to assess the pathological response to neoadjuvant chemotherapy in cases of locally advanced breast cancer.

### **Inclusion criteria**

1. Subjects above the age of 18.
2. Subjects with locally advanced cancer.
3. Ready for further communication.

### **Exclusion Criteria**

1. History of previous breast surgery
2. Previous radiation therapy for breast cancer
3. Metastatic illness

### **Methodology**

Individuals with malignant breast tumours older than eighteen years were evaluated. A core needle biopsy was used to confirm the diagnosis, and the grade and hormonal status were assessed. A metastatic workup was also carried out. Forty patients in all who satisfied the predetermined criteria were selected and sent for

neoadjuvant chemotherapy. Patients observed, and a modified radical mastectomy was carried out after the tumor's response was assessed clinically.

In order to evaluate the specimen's pathological reaction, analysis was performed, and observations were made <sup>[10, 11]</sup>.

**Result**

**Table 1:** Age distribution

<b>Age Groups</b>	<b>No. of individuals</b>	<b>Percentage</b>
30-40	4	10%
40-50	11	27%
50-60	13	33%
60-70	8	20%
70-80	4	10%
	40	100%

**Table 2:** Hormonal status

<b>Hormonal status</b>	<b>No. of individuals</b>	<b>Percentage</b>
Triple negative	7	17%
Triple positive	9	23%
ER/PR positive, HER2 Negative	17	43%
ER/PR negative, HER2 Positive	7	17%
	40	100%

**Table 3:** Chevalier classification

<b>Grade</b>	<b>No. of individuals</b>	<b>Percentage</b>
Grade 1	1	3%
Grade 2	5	13%
Grade 3	12	30%
Grade 4	22	53%
	40	100%

**Table 4:** Pathological response

<b>Response to NACT</b>	<b>No. of individuals</b>	<b>Percentage</b>
pCR	7	17%
nPR	33	83%
	40	100%

## Discussion

The prevalence of locally advanced or metastatic stages of the disease is high among patients in India. Several studies have demonstrated that the preponderance of breast cancer cases in Western nations are detected at stages I and II of the illness. Conversely, in India, a significant 45.7% of cases are documented at advanced stages. The predominant demographic of the study sample fell between the age bracket of 50-60<sup>[13]</sup>. Studies reveal that the condition is most commonly found in women from India, particularly between the ages of 40 and 50.<sup>[14, 15]</sup> Upon analysing age distribution patterns across multiple registers over a span of 5 years, it was seen that there was a significant increase in the proportion of individuals aged 45 to 49 years in all registries, except for the ones located in the northeastern region. Among the participants in the study, a total of 82 individuals, representing 60% of the entire population, were found to have been diagnosed with right-sided breast cancer<sup>[15, 16]</sup>. In contrast to the findings of Faidah Badru *et al*, who observed a greater incidence of left-sided invasive and in situ lesions, their results did not demonstrate statistical significance<sup>[17]</sup>. The study sample comprised 73% of people in stage IIIA and 27% of individuals in stage IIIB.

43% of participants exhibited a positive expression of oestrogen receptor (ER) and progesterone receptor (PR), while testing negative for human epidermal growth factor receptor 2 (HER2), as determined by the evaluation of hormonal status. In addition, 21% of individuals exhibited positive expression for all three receptors (ER, PR, and HER2), whereas 17% demonstrated negative expression for all three receptors. The existence of oestrogen receptor (ER) and progesterone receptor (PR) in invasive cancer is highly correlated with enhanced survival and acts as a key prognostic marker. Upon diagnosis, the majority of patients in India commonly exhibit locally advanced or metastatic stages. Several studies suggest that the majority of breast cancer cases in Western countries are detected during stages I and II of the disease. Conversely, in India, a significant proportion of cases, specifically 45.7%, are reported at advanced stages. Studies reveal that the condition is most commonly found in women from India, particularly between the ages of 40 and 50<sup>[15]</sup>. An examination of the 5-year age distribution patterns in all registries showed a significant increase in the relative number of adults aged 45 to 49 years in all registries, except for those in the northeastern region. Among the individuals included in the study, a total of 82 people, or 60% of the entire population, were found to have been diagnosed with right-sided breast cancer<sup>[16]</sup>.

In contrast to the non-significant results obtained by Faidah Badru *et al.*, this contradicts previous research that has documented a higher prevalence of left-sided invasive and in situ lesions<sup>[17]</sup>. The study population consisted of 73% individuals identified as stage IIIA and 27% individuals classed as stage IIIB. 43% of participants exhibited a positive expression of oestrogen receptor (ER) and progesterone receptor (PR), while testing negative for human epidermal growth factor receptor 2 (HER2), as determined by the evaluation of hormonal status. In addition, 21% of individuals exhibited positive expression for all three receptors (ER, PR, and HER2), whereas 17% displayed negative expression for all three receptors.

The proportion of cancers that tested positive for oestrogen receptor (ER) and progesterone receptor (PR) was 67% each, whereas the proportion of tumours that tested positive for (HER2) was 40%. Our research revealed a higher occurrence of ER

and PR positive status compared to previous studies, whereas the frequency of HER 2 positivity was consistent with past findings. The MRM specimen was evaluated and the pathological reaction was classified according to the Chevalier classification. The results showed that 3% of the reactions were grade 1, 13% were grade 2, 30% were grade 3, and 53% were grade 4. Out of all the research participants, a complete pathological response was observed in 17% of them, while the remaining 83% did not show any response. This corresponds to a response rate of 54.12<sup>[18, 19]</sup>. Previous research has shown that a pathological complete response (pCR) in the original tumour is found in 3% to 16% of persons with operable breast cancer and locally advanced breast cancer (LABC).

Individuals with lower or absent oestrogen receptor (ER) values demonstrated considerably higher rates of positive response to chemotherapy compared to individuals with higher ER values, as assessed through statistical analysis. Both Bonadonna *et al* and Mauriac *et al* have noted that in the neoadjuvant setting, tumours that lack oestrogen receptor (ER) expression are more likely to exhibit higher rates of response compared to tumours that express ER. The higher occurrence of oestrogen receptor (ER) positive cases may account for the lower rate of response to neoadjuvant chemotherapy seen in our study<sup>[19]</sup>.

### Conclusion

Locally advanced breast cancer (LABC) is a rare occurrence and presents a substantial clinical difficulty. Despite the implementation of combined-modality therapy and the use of innovative medications, the long-term disease-free survival rate still ranges from 50% to 70%. This suggests that the most effective treatment method for these individuals has not yet been achieved. Neo-adjuvant systemic therapy is the accepted treatment for locally advanced breast cancer (LABC) when used as part of a multimodality strategy. Extensive research has been conducted to determine the most effective chemotherapy regimen and duration for induction systemic chemotherapy. However, a consensus has not yet been reached. The NCT also placed significant emphasis on the significance of the early treatment response. This variable is a well acknowledged and significant element in clinical trials that investigate the utilisation of chemotherapy during the initial phases of treatment. The primary benefit of preoperative therapy is in its ability to evaluate the tumor's response and then customise subsequent treatment. However, there is currently no strong empirical evidence to support a notable connection between clinical and pathological responses.

Research has confirmed that achieving a pathological complete response (pCR) in the primary tumour is linked to better outcomes in terms of disease-free survival. Furthermore, patients who do not develop axillary lymph node metastases after receiving neoadjuvant chemotherapy also experience a higher chance of survival without disease recurrence. Identifying the tumours that are more prone to showing a favourable response to various medications and treatment methods could greatly enhance the prognosis. Customising the therapy of locally advanced breast cancer (LABC) involves integrating advancements in our understanding of cancer biology with genetic data, resulting in extremely effective therapies. Identifying the tumours that are most prone to showing a positive response to various medications and treatment methods has the potential to greatly enhance the prognosis. The management

of locally advanced breast cancer (LABC) can be tailored according to an individualised strategy that integrates advancements in our understanding of cancer biology and genetic profiling, resulting in exceptionally efficacious therapies.

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**Conflict of interest**

None

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