

ACCURACY OF SENTINEL LYMPH NODE BIOPSY AFTER NEOADJUVANT CHEMOTHERAPY IN LOCALLY ADVANCED BREAST CANCER: A PROSPECTIVE STUDY EVALUATING CLINICAL, RADIOLOGICAL, AND PATHOLOGICAL CORRELATION

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ABSTRACT

Background: To evaluate the predictive accuracy of sentinel lymph node biopsy (SLNB) following neoadjuvant chemotherapy (NACT) in patients with locally advanced breast cancer (LABC), and to assess the correlation between SLNB findings and clinical, imaging, and histopathological nodal status. **Materials and Methods:** This prospective observational study was conducted at a tertiary care center and included 109 female patients with LABC who received at least two cycles of NACT (CAF regimen). Clinical response was assessed using RECIST criteria. SLNB was performed intraoperatively using methylene blue dye, followed by axillary dissection. Data on SLNB identification rates, nodal downstaging, and correlations with ultrasonography (USG) and histopathology were analyzed. **Result:** SLNB was successfully performed in 49.54% of patients. Following NACT, 38.53% of patients achieved complete response, while 70.64% became clinically node-negative. There was no statistically significant correlation between SLNB positivity and pre-chemotherapy tumor stage ($p = 0.1006$). However, a significant concordance was observed between USG and histopathological nodal assessment ($p < 0.0001$). **Conclusion:** SLNB following NACT demonstrates moderate detection rates and variable reliability in predicting nodal status in LABC. While NACT effectively downstages axillary disease in a majority of patients, a multimodal approach—combining clinical assessment, imaging, and pathology—is essential for accurate staging. Further large-scale studies are needed to validate these findings.

INTRODUCTION

Breast cancer remains the most frequently diagnosed malignancy and the leading cause of cancer-related mortality among women globally. In 2022 alone, an estimated 2.3 million new cases were diagnosed, with over 670,000 deaths attributed to the disease worldwide.^[1] Although breast cancer can occur at any age after puberty, its incidence rises with age, particularly in women over 50 years. The disparity in incidence and mortality rates is particularly stark across regions of differing socioeconomic development: in high Human Development Index (HDI) countries, one in 12 women will be diagnosed with breast cancer during their lifetime, while one in

71 will succumb to it. Conversely, in low HDI countries, while the incidence is lower (1 in 27), mortality is higher, with one in 48 women dying from the disease.^[1]

The pathogenesis of breast cancer is multifactorial, encompassing both modifiable (e.g., lifestyle, reproductive history) and non-modifiable (e.g., genetics, age) risk factors. Molecular subtyping based on gene expression profiling categorizes breast cancer into Luminal A, Luminal B, HER2-enriched, triple-negative, and basal-like subtypes, each carrying distinct prognostic and therapeutic implications.^[2] Clinically, breast cancer may present as early-stage disease, locally advanced breast cancer (LABC), or metastatic disease. LABC is

characterized by involvement of the overlying skin or underlying pectoral musculature, often accompanied by regional lymphadenopathy.

Locoregional control in LABC has traditionally involved axillary lymph node dissection (ALND) following systemic neoadjuvant chemotherapy (NACT), which aims to downstage both the primary tumor and axillary nodal burden. However, ALND is associated with significant morbidity, including lymphedema, sensory neuropathy, and reduced shoulder mobility. In contrast, sentinel lymph node biopsy (SLNB) offers a less invasive yet accurate alternative for axillary staging, particularly in patients with a clinically negative axilla (cN0) post-NACT.^[3]

The sentinel lymph node (SLN)—the first node to receive lymphatic drainage from the primary tumor site—serves as a surrogate for regional nodal status. SLNB, performed using perilesional injection of blue dye or radiocolloid tracers, enables intraoperative identification and pathological assessment of the SLN. This approach allows for selective ALND only when macrometastases (>2 mm) are detected, thereby minimizing overtreatment.^[4] Adverse effects of SLNB are generally mild but may include hypersensitivity reactions, dye-related tissue discoloration, and transient fluid collections.

The American College of Surgeons Oncology Group (ACOSOG) Z0011 trial demonstrated that women with T1–T2 tumors and limited nodal involvement (1–2 positive SLNs) undergoing breast-conserving therapy and whole-breast irradiation could safely omit completion ALND without compromising survival outcomes.^[5] These findings have significantly reshaped axillary management in breast cancer. In light of the increasing breast cancer burden in Jharkhand, India, particularly among women presenting with LABC, this study evaluates the diagnostic accuracy of SLNB following NACT in predicting axillary nodal status. The aim is to determine whether SLNB can serve as a reliable staging modality to guide surgical decision-making and potentially obviate the need for ALND in select

patients treated at the Rajendra Institute of Medical Sciences (RIMS), Ranchi.

MATERIALS AND METHODS

This prospective observational study was conducted in the Department of General Surgery at RIMS, Ranchi, following Institutional Ethics Committee approval. Female patients over 20 years with locally advanced breast cancer who had received at least two cycles of CAF-based neoadjuvant chemotherapy were included. Exclusion criteria included recurrent cancer, pregnancy, methylene blue allergy, or planned breast-conserving surgery.

The sample size (n=109) was calculated based on a sensitivity of 94%, 10% confidence interval width, 5% alpha error, 80% power, and 20% prevalence. Eligible patients underwent clinical evaluation, bilateral breast and axillary ultrasound, trucut biopsy, abdominal ultrasound, baseline labs, chest/lumbar X-rays, and echocardiography. Tumor response was assessed using RECIST guidelines after each chemotherapy cycle.

Before surgery, informed consent and skin sensitivity testing for methylene blue dye were performed. Intraoperatively, 2 mL methylene blue was injected peritumorally; sentinel lymph nodes (SLNs) were visually identified and biopsied if stained, followed by axillary dissection.

Postoperative monitoring included assessment for allergic reactions, urine discoloration, seroma, and neurological symptoms. Data were collected from interviews and records, analyzed using SPSS v25. Categorical variables were reported as frequencies/percentages, with significance tested via Chi-square or Fisher's exact test (p<0.05).

RESULTS

The majority of patients were aged between 41–50 years, with a mean age of 49.37 years. Postmenopausal women accounted for 60.55% of the cases, while 39.45% were premenopausal. [Table 1]

Table 1: Demographic Characteristics of the Patients

| Category | Group | No. of patients | Percentage (%) |
|------------------|-----------------|-----------------|----------------|
| Age group | <30 | 1 | 0.92 |
| Age group | 30-40 | 21 | 19.27 |
| Age group | 41-50 | 41 | 37.62 |
| Age group | 51-60 | 27 | 24.77 |
| Age group | >60 | 19 | 17.42 |
| Menstrual status | Pre-menopausal | 43 | 39.45 |
| Menstrual status | Post-menopausal | 66 | 60.55 |

The most common presenting symptom was a combination of breast lump and pain. Right-sided

breast involvement was significantly more prevalent than left-sided involvement. [Table 2]

Table 2: Clinical Presentation of the Patients

| Category | Group | No. of patients | Percentage (%) |
|------------|--------------|-----------------|----------------|
| Symptoms | Lump | 28 | 25.69 |
| Symptoms | Pain | 19 | 17.42 |
| Symptoms | Both | 62 | 56.89 |
| Laterality | Left breast | 24 | 22.02 |
| Laterality | Right breast | 85 | 77.98 |
| Laterality | Both breasts | 0 | 0.0 |

More than half of the patients were diagnosed at T3 stage, with approximately equal distribution of node-

positive and node-negative disease at presentation. [Table 3]

Table 3: Tumor and Nodal Staging at Presentation

| Category | Group | No. of patients | Percentage (%) |
|--------------|----------|-----------------|----------------|
| T-staging | T1 | 0 | 0.0 |
| T-staging | T2 | 50 | 45.87 |
| T-staging | T3 | 58 | 53.21 |
| T-staging | T4 | 1 | 0.92 |
| Nodal status | Positive | 54 | 49.55 |
| Nodal status | Negative | 55 | 50.45 |

A complete clinical response was observed in 38.53% of patients, while 70.64% became clinically node-negative post-NACT. [Table 4]

Table 4: Response to Neoadjuvant Chemotherapy

| Category | Group | No. of patients | Percentage (%) |
|-----------------------|-------------|-----------------|----------------|
| Response to NACT | Complete | 42 | 38.53 |
| Response to NACT | Partial | 34 | 31.19 |
| Response to NACT | No response | 33 | 30.28 |
| Post-NACT Node Status | Positive | 32 | 29.36 |
| Post-NACT Node Status | Negative | 77 | 70.64 |

SLNB correlation with tumor stage, and comparison of nodal status assessed by ultrasonography versus histopathology. SLNB was positive in nearly half the

patients, and a statistically significant correlation was observed between HPE and USG findings. [Table 5,5a,5b,5c]

Table 5a: SLNB Detection Following Neoadjuvant Chemotherapy

| SLNB after NACT | No. of patients | Percentage (%) |
|-----------------|-----------------|----------------|
| Positive | 54 | 49.54 |
| Negative | 55 | 50.46 |

Table 5b: SLNB Correlation with Tumor Stage

| Pre-chemotherapy clinical TNM staging | SLNB Positive | SLNB Negative | p-value |
|---------------------------------------|---------------|---------------|---------|
| T2 (n=50) | 20 | 30 | 0.1006 |
| T3/T4 (n=59) | 34 | 25 | 0.1006 |

Table 5c: Correlation Between HPE and USG Nodal Status

| HPE nodal status | USG Positive | USG Negative | p-value |
|------------------|--------------|--------------|---------|
| Positive (n=54) | 41 | 13 | <0.0001 |
| Negative (n=55) | 2 | 53 | <0.0001 |

DISCUSSION

In this prospective study involving 109 patients with locally advanced breast cancer (LABC), the most frequently affected age group was 41–50 years, with a mean age of 49.37 years. This finding is consistent with global epidemiologic trends which indicate that breast cancer incidence peaks in midlife, particularly in regions with improving life expectancy and health awareness.^[1] Postmenopausal women comprised 60.55% of the study population, supporting previous findings that postmenopausal status is a well-established risk factor for breast cancer.^[2,3]

Most patients presented to the hospital within six months of the onset of symptoms, although some presented after more than a year, highlighting persistent delays in health-seeking behavior. The majority (56.89%) presented with both breast lump and pain. These clinical presentations align with typical manifestations of breast cancer described in literature, where lump is the most common initial complaint.^[4] Right breast involvement was observed

in 77.98% of cases, which differs from some Western studies that report a slight left-side predominance. Such variation may be influenced by genetic, environmental, or anatomical factors and warrants further investigation.^[5]

In terms of tumor stage, 53.21% of patients had T3 tumors and 45.87% had T2 tumors at presentation. This reflects the advanced disease burden commonly seen in resource-limited settings and underlines the need for early detection programs.^[6,7] Initial clinical nodal evaluation revealed that 49.55% of patients were node-positive, comparable to previous studies on LABC cohorts.^[8]

Following 1–2 cycles of neoadjuvant chemotherapy (CAF regimen), complete clinical response was observed in 38.53% of patients, partial response in 31.19%, and no response in 30.28%. A total of 70.64% of patients converted to node-negative status after chemotherapy, consistent with RECIST-guided response assessments reported in earlier trials.^[9] These findings reinforce the role of NACT in

downstaging axillary disease in node-positive breast cancer.^[10]

Sentinel lymph node biopsy (SLNB) was successful in 49.54% of patients post-NACT. Although lower than identification rates typically reported in early-stage breast cancer (95–98%),^[11] this reduced detection is in line with previously published studies showing decreased SLN identification post-chemotherapy due to lymphatic disruption.^[12,13] Notably, all patients in this study underwent axillary lymph node dissection, as intraoperative frozen section was not utilized. Among T2 patients, 40% were SLN-positive post-chemotherapy, while 57.6% of T3/T4 patients were SLN-positive. Although not statistically significant ($p = 0.1006$), this trend suggests higher residual axillary disease burden in patients with more advanced tumors, a pattern previously described in neoadjuvant trials.^[14]

A statistically significant correlation ($p < 0.0001$) was observed between post-chemotherapy ultrasonographic (USG) nodal status and histopathological evaluation. Of the 54 histopathologically positive cases, 41 were also detected by USG, while 13 were missed. The false-negative and false-positive rates highlight the limitations of imaging alone for nodal staging, consistent with prior findings that support histopathological confirmation as the diagnostic gold standard.^[15]

CONCLUSION

This study evaluated the accuracy of sentinel lymph node biopsy (SLNB) after neoadjuvant chemotherapy (NACT) in patients with locally advanced breast cancer (LABC). SLNB was successfully performed in 49.54% of cases; however, its correlation with pre-treatment tumor staging was not statistically significant. NACT effectively

downstaged axillary disease in the majority of patients, with over 69% showing clinical response and 70.64% achieving node-negative status.

A strong correlation between ultrasonography and histopathology ($p < 0.0001$) supports the use of imaging as an adjunct to guide axillary management. While SLNB shows promise, its limitations post-NACT underscore the need for a multimodal, individualized approach.

Larger, multicenter studies are needed to validate these findings and assess the long-term impact on recurrence and survival.

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