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CLINICAL OUTCOMES OF ANTHRACYCLINE-BASED NEOADJUVANT CHEMOTHERAPY FOLLOWED BY MODIFIED RADICAL MASTECTOMY IN PATIENTS WITH LOCALLY ADVANCED BREAST CARCINOMA: A PROSPECTIVE OBSERVATIONAL STUDY

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ABSTRACT

Background: Locally advanced breast carcinoma (LABC) remains a major challenge in developing countries because many patients present at an advanced stage due to delayed diagnosis, poor awareness, and limited screening facilities. Neoadjuvant chemotherapy (NACT) has become the standard initial treatment for LABC because it reduces tumour size, improves operability, and facilitates complete surgical excision. Anthracycline-based chemotherapy remains widely used because of its proven efficacy, affordability, and acceptable toxicity profile.

Aim: To evaluate the clinical outcomes, chemotherapy-related toxicities, surgical outcomes, and short-term oncological results of anthracycline-based neoadjuvant chemotherapy followed by modified radical mastectomy in patients with locally advanced breast carcinoma.

Methods: This prospective observational study included 100 female patients aged 45–70 years with Stage IIIA–IIIC breast carcinoma confirmed by clinical examination, sonomammography, and fine-needle aspiration cytology. All patients received three cycles of doxorubicin and cyclophosphamide administered every 21 days followed by modified radical mastectomy. Postoperative chemotherapy, radiotherapy and endocrine therapy were administered according to receptor status. Patients were followed for two years to evaluate tumour response, postoperative complications, recurrence, metastasis, and mortality.

Results: Among the 100 enrolled patients, 97 completed treatment and follow-up. Partial clinical response was achieved in 80 patients (82.5%), whereas 17 patients (17.5%) showed no significant response. No complete clinical response or disease progression was observed. Nausea and alopecia occurred in all patients. Vomiting occurred in 40%, generalized weakness requiring admission in 20%, febrile illness in 30%, urinary tract infection in 20%, and chemotherapy extravasation in 5%. Histopathological examination demonstrated invasive ductal carcinoma in 72.2% of patients. Seroma was the most common postoperative complication. No local recurrence was observed during two years of follow-up, while three patients developed distant metastasis and five patients died due to disease progression.

Conclusion: Anthracycline-based neoadjuvant chemotherapy followed by modified radical mastectomy provides satisfactory tumour downstaging, acceptable toxicity, and excellent locoregional disease control in patients with locally advanced breast carcinoma.

Keywords: Breast Carcinoma, Locally Advanced Breast Cancer, Neoadjuvant Chemotherapy, Modified Radical Mastectomy, Anthracycline, Doxorubicin.

INTRODUCTION

www.ajmrhs.com
eISSN: 2583-7761

Date of Received: 28-06-2026
Date Acceptance: 10-07-2026
Date of Publication: 16-07-2026

Breast cancer is the most common malignancy among women worldwide and remains one of the leading causes of cancer-related mortality. According to the Global Cancer Observatory (GLOBOCAN), breast cancer accounts for approximately one in four cancers diagnosed in women and represents a major public health burden **[1]**. In India, the incidence of breast cancer has increased steadily over the past two decades, with many patients presenting at an advanced stage

because of poor awareness, socioeconomic barriers, and lack of organised screening programmes **[2,3]**.

Locally advanced breast carcinoma (LABC) includes Stage III tumours characterised by large primary lesions, skin or chest wall involvement, and regional lymph node metastasis without distant spread **[4]**. Historically, surgery alone was associated with high rates of recurrence and poor survival. The introduction of neoadjuvant chemotherapy has significantly improved treatment outcomes by reducing tumour size, increasing operability, and eliminating occult micrometastatic disease **[5,6]**.

Anthracycline-based regimens containing doxorubicin and cyclophosphamide continue to be widely used because of their effectiveness and affordability, particularly in resource-limited settings **[7]**. Following tumour downstaging, modified radical mastectomy remains the preferred surgical procedure for patients with extensive breast involvement, multicentric disease, or residual tumour after chemotherapy. Adjuvant radiotherapy and endocrine therapy further reduce recurrence and improve survival in appropriately selected patients **[8–10]**.

Despite advances in multimodality treatment, distant metastasis remains the leading cause of mortality among patients with LABC. Therefore, evaluation of clinical response, treatment-related complications, postoperative outcomes, and follow-up remains essential for assessing treatment effectiveness **[11,12]**.

The present study was undertaken to evaluate the clinical outcomes of anthracycline-based neoadjuvant chemotherapy followed by modified radical mastectomy in patients with locally advanced breast carcinoma treated at a tertiary care teaching hospital.

Aim

To evaluate the clinical outcomes of anthracycline-based neoadjuvant chemotherapy followed by modified radical mastectomy in patients with locally advanced breast carcinoma.

Objectives

1. To evaluate the clinical response following neoadjuvant chemotherapy.
2. To assess chemotherapy-related adverse effects.
3. To study postoperative complications following modified radical mastectomy.
4. To evaluate histopathological findings and receptor status.
5. To assess recurrence, distant metastasis, and mortality during two-year follow-up.

MATERIALS AND METHODS

Study Design and Setting

This prospective observational study was conducted in the Department of General Surgery at a tertiary care teaching hospital over a two-year period from January 2024 To January 2026. The study aimed to evaluate the clinical outcomes of anthracycline-based neoadjuvant chemotherapy followed by modified radical mastectomy in patients with locally advanced breast carcinoma (LABC). Institutional Ethics Committee approval was obtained before commencement of the study, and written informed consent was obtained from all participants. The study adhered to the ethical principles of the Declaration of Helsinki [13].

Study Population

A total of 100 consecutive female patients aged 45–70 years with cytologically confirmed locally advanced breast carcinoma were prospectively enrolled. Diagnosis was established through clinical examination, bilateral sonomammography, and fine-needle aspiration cytology (FNAC). Clinical staging was performed according to the American Joint Committee on Cancer (AJCC) 8th edition TNM classification [14].

Inclusion Criteria

Patients fulfilling the following criteria were included:

- Female patients aged 45–70 years.
- Cytologically confirmed carcinoma breast by FNAC.
- Clinical Stage IIIA, IIIB, or IIIC disease.
- No evidence of distant metastasis.
- Patients fit to receive neoadjuvant chemotherapy and surgery.
- Written informed consent.

Exclusion Criteria

Patients were excluded if they had:

- Stage I, II, or IV breast carcinoma.
- Previous chemotherapy, radiotherapy, or breast surgery.
- Pregnancy or lactation.
- Severe cardiac, hepatic, or renal dysfunction contraindicating anthracycline therapy.
- Refusal to participate in the study.

Clinical Evaluation

A detailed history was obtained regarding duration of breast lump, pain, nipple discharge, ulceration, family history of breast cancer, menstrual and reproductive history, and associated comorbidities.

General and systemic examinations were performed in all patients. Local breast examination included assessment of tumour size, breast quadrant involved, skin changes, nipple retraction, chest wall fixation, and axillary or supraclavicular lymph node involvement.

Five patients presented with ulcerated breast lesions, while one patient had diffuse right upper limb oedema due to compression of the axillary vein by metastatic lymph nodes.

Image Showing Locally Advanced Carcinoma of Left Breast

Baseline Investigations

All patients underwent the following investigations before treatment:

- Complete blood count
- Random blood sugar
- Liver function tests
- Renal function tests
- Chest radiograph
- Bilateral sonomammography
- Ultrasonography of the abdomen and pelvis
- Electrocardiography
- FNAC of the breast lesion

Additional imaging was performed whenever clinically indicated.

Neoadjuvant Chemotherapy

All patients received **three cycles** of anthracycline-based chemotherapy consisting of:

- **Doxorubicin**
- **Cyclophosphamide**

Chemotherapy cycles were administered every 21 days after confirmation of adequate haematological and biochemical parameters.

Supportive treatment included antiemetics, proton pump inhibitors, hydration, nutritional advice, antibiotics when required, and recombinant human granulocyte colony-stimulating factor (rhG-CSF) for chemotherapy-induced neutropenia.

Response Assessment

Clinical response was assessed after completion of three chemotherapy cycles by physical examination and repeat imaging. Patients were classified as having:

- Complete response
- Partial response
- Stable disease (non-response)
- Progressive disease

Patients with operable disease subsequently underwent definitive surgery.

Surgical Management

Following neoadjuvant chemotherapy, 97 evaluable patients underwent modified radical mastectomy (MRM) under general anaesthesia. The procedure included complete removal of breast tissue with preservation of the pectoralis major muscle and Level I–II axillary lymph node dissection. Closed suction drains were placed routinely before wound closure.

All surgical specimens were sent for histopathological examination and immunohistochemistry.

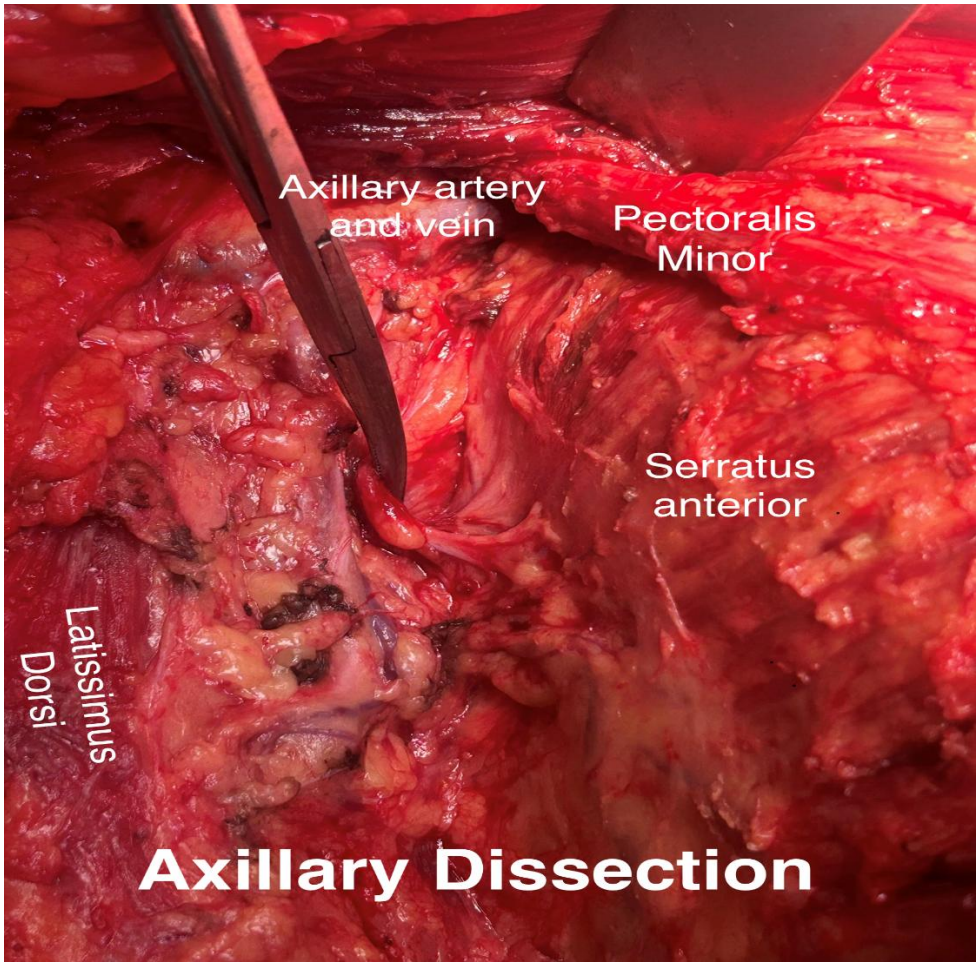

Image Showing Axillary Dissection

Histopathological Evaluation

Histopathological assessment included tumour type, grade, lymphovascular invasion, nodal status, and surgical margins.

Immunohistochemistry was performed for:

- Estrogen receptor (ER)
- Progesterone receptor (PR)
- HER2/neu receptor

Hormone receptor-positive patients subsequently received adjuvant endocrine therapy according to menopausal status.

Postoperative Treatment and Follow-up

All patients were referred for postoperative radiotherapy. Premenopausal women received tamoxifen (20 mg/day), whereas postmenopausal women received letrozole (2.5 mg/day) when indicated.

Patients were followed for two years with regular clinical examinations and appropriate laboratory and radiological investigations to assess recurrence, distant metastasis, postoperative complications, and survival. After completion of the study, patients were advised follow-up every three months for two years, then every six months for two years and annually thereafter.

Outcome Measures

The primary outcome was clinical response following neoadjuvant chemotherapy.

Secondary outcomes included chemotherapy-related toxicity, postoperative complications, histopathological findings, receptor status, local recurrence, distant metastasis, and mortality.

Statistical Analysis

Data were entered into Microsoft Excel and analysed using IBM SPSS Statistics version 25.0. Continuous variables were expressed as mean ± standard deviation, whereas categorical variables were presented as frequencies and percentages. A p-value <0.05 was considered statistically significant [15].

RESULTS

A total of 100 female patients with locally advanced breast carcinoma were enrolled in the study. Three patients were lost to follow-up after completion of neoadjuvant chemotherapy; therefore, 97 patients completed treatment and were included in the final outcome analysis. The results are summarized below.

Age Distribution

Figure 1. Age Distribution of Patients

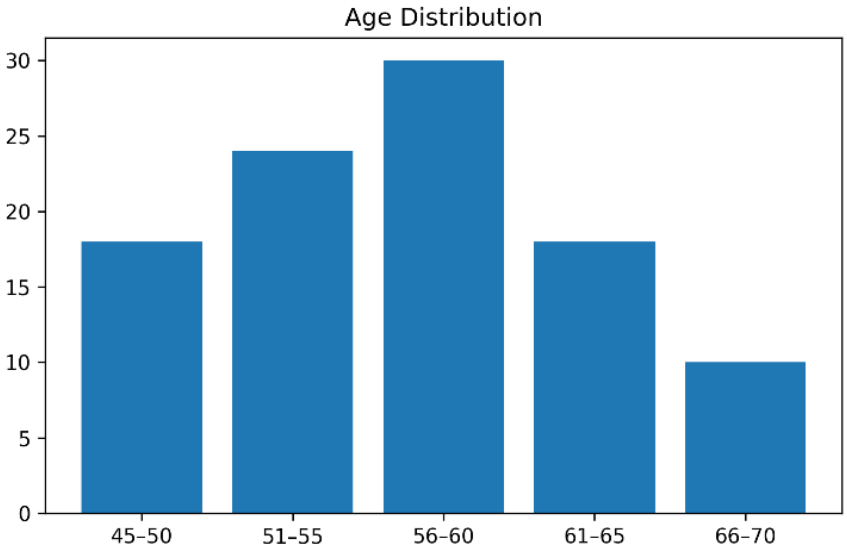

Figure Legend: Bar diagram showing the age distribution of patients included in the study.

Summary

The majority of patients belonged to the 51–60-year age group (54%), with the highest frequency observed in patients aged 56–60 years (30%). The remaining patients were distributed across the 45–50, 61–65, and 66–70-year age groups. These findings are comparable with Indian epidemiological studies demonstrating a higher incidence of breast carcinoma during the fifth and sixth decades of life [1,2].

Clinical Stage Distribution

Figure 2. Clinical Stage at Presentation

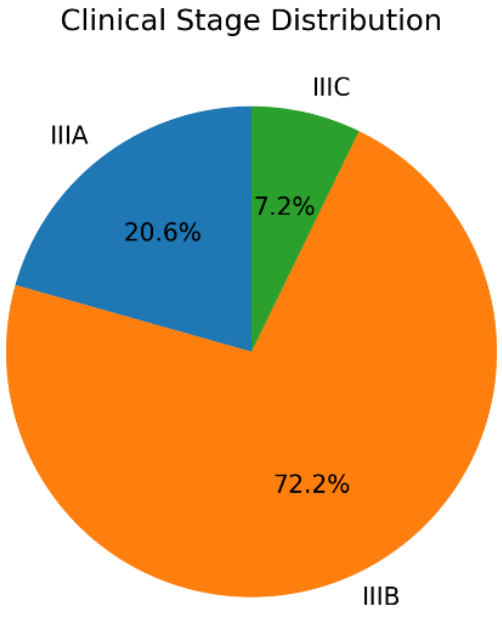

Figure Legend: Pie chart illustrating the distribution of AJCC Stage III breast carcinoma.

Summary

Most patients presented with Stage IIIB disease (70 patients; 72.2%), followed by Stage IIIA (20 patients; 20.6%) and Stage IIIC (7 patients; 7.2%). The predominance of Stage IIIB disease reflects delayed diagnosis and late presentation, which

remain common in developing countries because of limited screening and delayed healthcare access [2,4,14].

Clinical Response to Neoadjuvant Chemotherapy
Figure 3. Clinical Response Following Neoadjuvant Chemotherapy

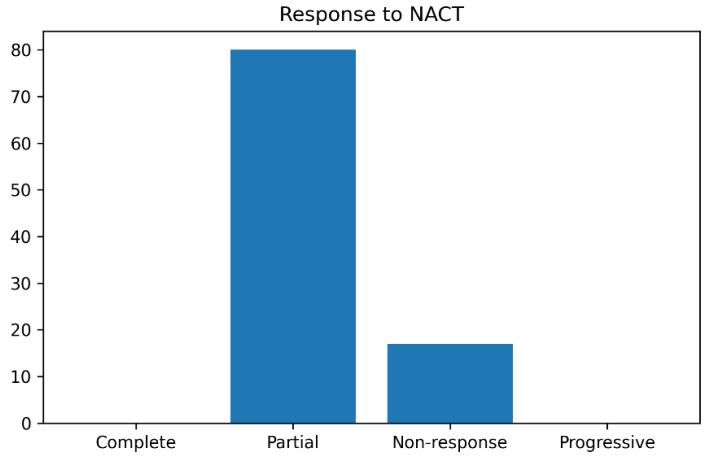

Figure Legend: Bar diagram showing treatment response after three cycles of anthracycline-based neoadjuvant chemotherapy.

Summary
Among the **97 evaluable patients**, **80 patients (82.5%)** demonstrated a **partial clinical response**, while **17 patients (17.5%)** had no significant reduction in tumour size. No patient achieved complete clinical response or developed progressive disease during treatment. The high rate of partial response indicates effective tumour downstaging, facilitating definitive surgical management **[5–8]**.

Chemotherapy-Related Complications
Figure 4. Chemotherapy-Related Adverse Effects

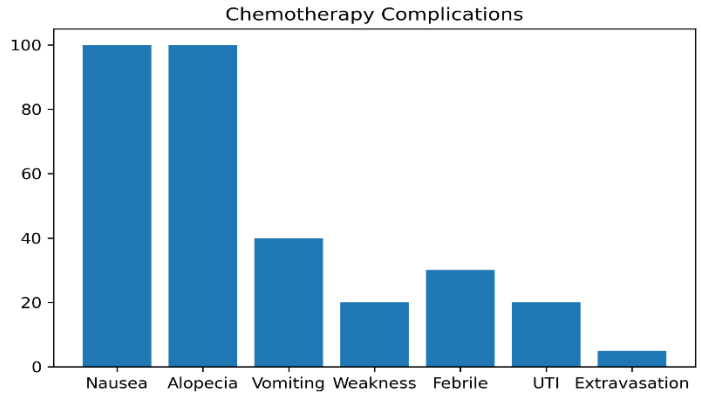

Figure Legend: Horizontal bar diagram illustrating chemotherapy-related complications observed during treatment.

Summary
All patients completed the planned three cycles of chemotherapy. Nausea and alopecia occurred in all patients (100%). Vomiting was observed in 40 patients (40%) and was managed with oral antiemetics, proton pump inhibitors (PPIs), antacids, hydration, and supportive care. Generalized weakness requiring short-term hospital admission occurred in 20 patients (20%) and improved with intravenous fluids, PPIs, nutritional supplementation, and conservative management.
Additional complications included febrile illness in 30 patients (30%), urinary tract infection in 20 patients (20%), chemotherapy extravasation with cellulitis in five patients (5%), and neutropenia, which was the most common haematological toxicity and responded well to recombinant human granulocyte colony-stimulating factor (rhG-CSF).

No chemotherapy-related mortality occurred, and all patients completed treatment as planned [11,12].

Surgical Outcomes

Following neoadjuvant chemotherapy, 97 patients underwent modified radical mastectomy (MRM). Surgery was successfully completed in all patients without intraoperative mortality. Histopathological examination and immunohistochemistry were performed for all surgical specimens.

Histopathological Distribution

Figure 5. Histopathological Types of Breast Carcinoma

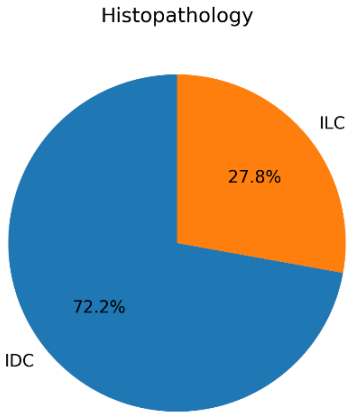

Figure Legend: Pie chart demonstrating the histopathological distribution of breast carcinoma.

Summary

Histopathological examination showed invasive ductal carcinoma (IDC) in 70 patients (72.2%), whereas 27 patients (27.8%) had invasive lobular carcinoma (ILC). IDC was the predominant histological subtype, consistent with previously published epidemiological studies [13].

Hormone Receptor Status

Figure 6. Distribution of Hormone Receptor Status

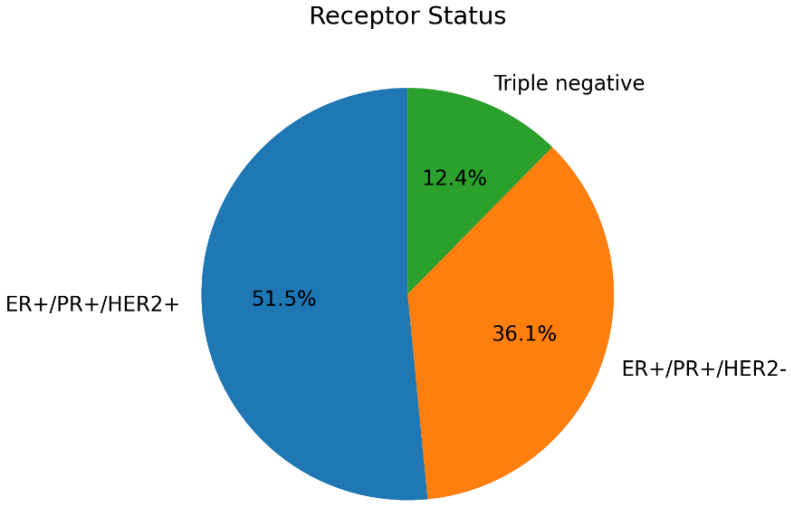

Figure Legend: Pie chart illustrating ER, PR, and HER2 receptor status.

Summary

Immunohistochemistry demonstrated ER+/PR+/HER2-positive tumours in 50 patients (51.5%), ER+/PR+/HER2-negative tumours in 35 patients (36.1%), and triple-negative breast cancer in 12 patients (12.4%). Hormone receptor positivity in the majority of patients supported the use of adjuvant endocrine therapy after surgery [9,10].

Postoperative Complications
Figure 7. Postoperative Complications

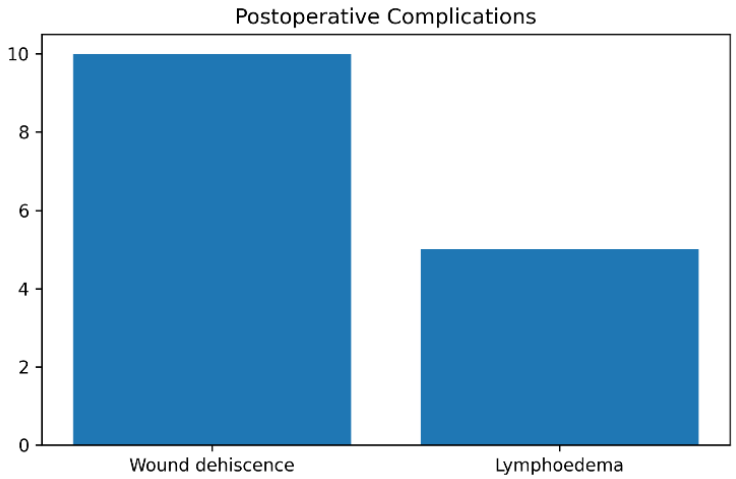

Figure Legend: Bar diagram showing postoperative complications following modified radical mastectomy.

Summary
Seroma was the most common postoperative complication and was managed with prolonged closed suction drainage. Wound dehiscence occurred in 10 patients (10.3%) and healed with regular dressings followed by secondary suturing. Mild ipsilateral upper-limb lymphoedema developed in five patients (5.2%) and improved with physiotherapy and compression therapy. No patient required reoperation because of postoperative complications [16].

Follow-Up Outcomes
Figure 8. Two-Year Follow-Up Outcomes

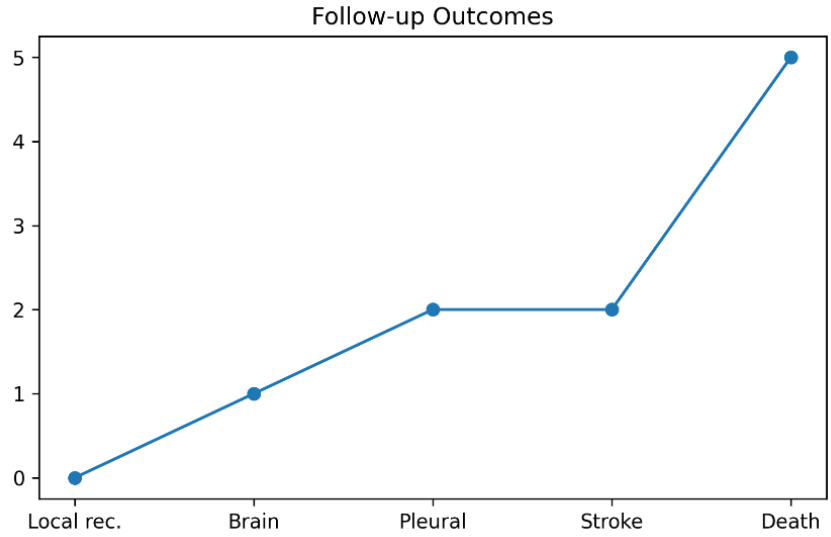

Figure Legend: Line diagram showing oncological outcomes during the two-year follow-up period.

Summary
During the two-year follow-up, no local recurrence was observed, indicating excellent locoregional disease control following multimodality treatment. Three patients (3.1%) developed distant metastases, including one patient with brain metastasis and two patients with pleural metastasis. Two patients experienced cerebrovascular accidents (stroke) during follow-up. Overall, five patients died because of metastatic disease and associated complications. These findings suggest that while multimodality treatment provides effective local control, distant metastasis remains the major determinant of long-term survival [6,7,17].

Overall Treatment Outcome
Anthracycline-based neoadjuvant chemotherapy achieved satisfactory tumour downstaging in the majority of patients, allowing definitive surgical

treatment in all evaluable cases. Combined treatment with chemotherapy, modified radical mastectomy, postoperative radiotherapy, and endocrine therapy resulted in excellent locoregional disease control with acceptable treatment-related toxicity. Nevertheless, distant metastatic disease remained the principal cause of mortality during the two-year follow-up period [7, 18–20].

DISCUSSION

Locally advanced breast carcinoma (LABC) remains a major health problem in developing countries because a large proportion of patients present with advanced disease. Delayed diagnosis, poor awareness, socioeconomic constraints, and limited screening programmes contribute significantly to late presentation **[1–3]**. The present prospective observational study evaluated the outcomes of anthracycline-based neoadjuvant chemotherapy followed by modified radical mastectomy and demonstrated favourable tumour downstaging, acceptable treatment-related toxicity, and excellent short-term locoregional disease control.

The majority of patients in the present study were between 51 and 60 years of age, which is consistent with Indian cancer registry data and previously published studies reporting the highest incidence of breast cancer during the fifth and sixth decades of life [2,3]. Unlike Western countries, breast cancer in India frequently presents at a younger age and at a more advanced stage, emphasizing the need for improved awareness and early detection strategies.

Stage IIIB disease constituted the largest proportion of patients in this study. Similar findings have been reported in other Indian series, where delayed presentation remains common because of inadequate screening and delayed healthcare access [3,4]. Advanced-stage disease is associated with larger tumour size, increased nodal involvement, and a higher risk of distant metastasis.

Neoadjuvant chemotherapy has become the standard initial treatment for LABC because it reduces tumour size, improves operability, and allows assessment of tumour response [5–7]. In the present study, 82.5% of evaluable patients achieved a partial clinical response, while 17.5% showed no significant response. No patient demonstrated disease progression during treatment. These findings are comparable with the NSABP B-18 and NSABP B-27 trials, which demonstrated significant tumour downstaging and improved operability following anthracycline-based neoadjuvant chemotherapy [6,7].

No complete clinical response was observed in the present study. This may be attributed to the advanced stage of disease at presentation and the use of three cycles of anthracycline-based chemotherapy without sequential taxane therapy. Contemporary regimens incorporating taxanes and HER2-targeted therapy have demonstrated higher pathological complete response rates, particularly among HER2-positive and triple-negative breast cancers [8–10].

Treatment-related adverse effects were generally manageable. Nausea and alopecia occurred in all patients, whereas vomiting, generalized weakness requiring admission, febrile illness, urinary tract infection, neutropenia, and chemotherapy extravasation responded well to supportive treatment. Importantly, no chemotherapy-related mortality occurred. These findings are consistent with the established toxicity profile of anthracycline-containing regimens and highlight the importance of supportive care during chemotherapy [11,12].

Histopathological examination identified invasive ductal carcinoma as the predominant tumour subtype, accounting for 72.2% of cases, followed by invasive lobular carcinoma. This distribution is consistent with international epidemiological studies [13]. Hormone receptor-positive disease predominated, allowing administration of adjuvant endocrine therapy with tamoxifen or letrozole according to menopausal status. Endocrine therapy has been shown to significantly reduce recurrence and improve survival in hormone receptor-positive breast cancer [14,15].

Seroma was the most common postoperative complication, followed by wound dehiscence and mild lymphoedema. All complications were managed successfully using standard postoperative care, including prolonged drainage, wound care, physiotherapy, and compression therapy. These findings are comparable with previously published surgical series [16].

An important finding of the present study was the absence of local recurrence during the two-year follow-up period, indicating excellent locoregional control following multimodality treatment. However, three patients developed distant metastases, and five patients died due to metastatic disease and its complications. These findings suggest that while surgery and local treatment effectively control the primary tumour, systemic dissemination remains the major determinant of long-term survival [17–20].

Overall, the present study demonstrates that anthracycline-based neoadjuvant chemotherapy followed by modified radical mastectomy remains an effective and practical treatment strategy for patients with LABC, particularly in resource-limited settings where access to newer targeted therapies may be limited.

Strengths of the Study

- Prospective observational study.
- Uniform chemotherapy protocol for all patients.
- Standardized surgical management with modified radical mastectomy.

- Complete histopathological and immunohistochemical evaluation.
- Structured two-year follow-up assessing recurrence, metastasis, complications, and mortality.

Limitations of the Study

The study was conducted at a single tertiary care centre with a relatively small sample size. The follow-up period of two years was insufficient to evaluate long-term disease-free and overall survival. Three patients were lost to follow-up after neoadjuvant chemotherapy, and molecular biomarkers beyond ER, PR, and HER2 were not routinely assessed. Larger multicentre studies with longer follow-up are recommended.

CONCLUSION

Anthracycline-based neoadjuvant chemotherapy followed by modified radical mastectomy is an effective treatment strategy for patients with locally advanced breast carcinoma. The treatment achieved satisfactory tumour downstaging, enabling definitive surgery in all evaluable patients, with acceptable treatment-related toxicity and excellent locoregional disease control. Although distant metastasis remained the principal cause of mortality, the overall outcomes support the continued use of anthracycline-based neoadjuvant chemotherapy in resource-limited settings. Further multicentre studies with longer follow-up are required to evaluate long-term survival outcomes and optimise treatment strategies.

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How to cite this article: Linganagouda S Patil, Gayatri L Patil, Nikhil M, Shiva Sai, CLINICAL OUTCOMES OF ANTHRACYCLINE-BASED NEOADJUVANT CHEMOTHERAPY FOLLOWED BY MODIFIED RADICAL MASTECTOMY IN PATIENTS WITH LOCALLY ADVANCED BREAST CARCINOMA: A PROSPECTIVE OBSERVATIONAL STUDY, Asian J. Med. Res. Health Sci., 2026; 4 (2):2245-2254.

Source of Support: Nil, Conflicts of Interest: None declared.