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Original Research Article

Clinical study of outcome of operative management of locally advanced breast carcinoma after neoadjuvant chemotherapy at tertiary care hospital

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ABSTRACT

Background: Locally advanced diseased of the breast is characterised clinically by features suggesting infiltration of the skin or chest wall by tumour or matted involved axillary nodes (AJCC-stage III). Successful reduction in the size of the tumor is associated with increased rate of operability i.e., modified radical mastectomy or breast conserving therapy (BCT). The aim of this study is to assess outcome of surgery in management of locally advanced breast carcinoma (LABC) after neoadjuvant chemotherapy.
Methods: It is an observational retrospective study of 40 cases of LABC admitted at general surgery department.
Results: The response to neoadjuvant chemotherapy was seen in 92.5% cases- with complete response in 10% cases (4 patients) and partial response in 82.5% (33 patients). No response was observed in 7.5% cases (3 patients) after 4 cycles of neoadjuvant chemotherapy. All patients were subjected to surgery after chemotherapy, out of whom 02 patients (5%) have surgical site infection and flap necrosis in 01 patient (2.5%) and no mortality; 02 patients subjected to toilet mastectomy without neoadjuvant chemotherapy resulted in 01 recurrence within 6 months of completion of adjuvant therapy and 01 death postoperatively.
Conclusions: Majority of patients were subjected to neoadjuvant chemotherapy responded partially to it. Overall observations suggested that most of the LABC responds to neoadjuvant chemotherapy with minimum post-operative morbidity and mortality.

Keywords: Breast, Carcinoma, Locally advanced carcinoma, Management of breast cancer

INTRODUCTION

Locally advanced diseased of the breast is considered clinically by structures suggesting infiltration of the skin or chest wall by tumour or matted involved axillary nodes (AJCC- stage III). Enormous operable breast cancer should not be reflected as locally advanced. Median survival is about 2-2.5 years, which is parallel to that described in the 19th and early 20th centuries.[1,2] Breast cancer is the most communal cancer diagnosed in women globally with over 1.3 million new cases per year. It is predictable that in 2008 there were 115251 new cases of breast cancer with an age-standardized incidence rate (ASIR) of 22.9 per 100000. It is probable that by 2030 no. new cases of breast cancer in India will extent just under 200000 per year.[3] Carcinoma of breast ensues frequently in the Western world, accounting for 3-5% of all deaths in women. In developing countries, it accounts for 1-3% of deaths.[4] Difference between Far Eastern and Western countries is shrinking but is still about fivefold.[5]

LABC presents with problematic management delinquent. It remains a challenge to achieve local and

distant control of LABC. Over last decade preoperative/ neoadjuvant chemotherapy has arisen as the standard of care for these patients. Successful lessening in size of tumor is associated with augmented rate of operability i.e., modified radical mastectomy or BCT. Also no. of cases with stage III with sepsis and severe local infection measured for toilet mastectomy followed by adjuvant chemotherapy and/ hormonal therapy. In hospital which gratifies to patients of urban and rural part of district, delay in initial presentation was common. For patients present at later stage with more advanced malignancy, treatment of such patients is perplexing. So, present study carried out to assess outcome of operative management of LABC after neo-adjuvant chemotherapy.

METHODS

It is observational retrospective study of 40 cases of LABC admitted at general surgery department, new civil hospital, Surat, South Gujarat from May 2020 to April 2021. Institutional ethical permission taken prior to study.

Inclusion criteria

All breast carcinoma indoor patients presenting at our hospital, of any age with-Female patients of locally advanced carcinoma breast with age group of 20-60 years, females who has taken chemotherapy and radiotherapy in NCH, Surat, such cases span stage IIIA, stage IIIB and stage IIIC of AJCC classification of breast carcinoma included in the study.

Exclusion criteria

Females of stage 1, stage 2 and stage 4 carcinoma breast. Age<20 and age>60 years, females who has taken chemotherapy and radiotherapy from other hospitals excluded from the study.

Following data were collected and analysed from indoor case sheets retrieved from central record section of the hospital. Findings of clinical examination, laboratory, radiology and pathological examination.

Epidemiological information and patient's bio-data, clinical findings like tumor morphology and systemic manifestations (metastatic clinical evidences like headache, chest, abdominal pain and distention, bone pains etc.

Radiological findings of sono-mammography, X-rays, bone scan and PET scan; ECG and 2-D ECHO findings. Histopathological findings of true cut biopsy and receptor status for ER, PR and HER 2 neu. Clinical staging after above clinical and investigative findings as per AJCC (2002).

At our institute patients were subjected to at least 3-4 cycles of neoadjuvant chemotherapy according to response assessed by oncosurgeons and oncophysicians. During this period, response to chemotherapy were assessed along with its complications and noted in the indoor case sheets were entered in study proformas. Following neoadjuvant chemotherapy patients were subjected to modified radical mastectomy and its outcome in form of postoperative morbidity and mortality were noted. Follow up findings from OPD case sheets of patients included in this study during study period were collected and analysed.

Data entry and analysis

The data was entered in MS excel sheet and analysed using SPSS software. Qualitative data were described as a frequency and percentages, while quantitative data were described as mean and standard deviation.

RESULTS

The age of patients ranged between 20 and 60 years (mean 45 years). On distribution of cases according to gonadal activity. At first visit 37.5% cases were premenopausal while 62.5% were postmenopausal. Out of total, 67.5% Patients had stage 3a, followed by 32.5% cases had stage 3b as per tumor staging; as per size of Tumor-T3 (56.6%) while T2 and T4 were 26.6% and 16.6 respectively. Among the study participants, majority 62.5% cases had N1 Nodal staging in this study; Out of 40 cases, 10 patients were ER, PR +ve with Her2 –ve. While ER-ve PR -ve Her2 +ve cases were 8 and Triple negative cases were 7. Total 3 case were only PR +ve. Among the 12 patients' investigation regarding receptor was not done. The response to neoadjuvant chemotherapy was seen in 92.5% cases-with complete response seen in 10% cases (4 patients) and partial response was seen 82.5% (33 patients). No Response with was observed in 7.5% cases (3 patients) after 4 cycles of neoadjuvant chemotherapy. After completion of 4 cycles of chemotherapy if response is good in form of reduction in size of tumor with no positive axillary nodes, patients can be given option of breast conservation surgery [down stage to stage II (AJCC 2002)]. In our study no patient were included in breast conservation surgery. All patients were subjected to surgery (Modified radical mastectomy) after completion of 4 cycles of chemotherapy. We encountered surgical site infection in 02 patients (5%), Flap necrosis in 01 patient (2.5%); 02 patients subjected to toilet mastectomy without neoadjuvant chemotherapy resulted in 01 recurrence within 6 months of completion of adjuvant therapy and 01 death postoperatively.

Table 1: Age group wise distribution of Study participants, (n=40).

Age (Years)	Frequency (%)
21-30	0 (0)
31-40	9 (22.5)
41-50	26 (65)
51-60	5 (12.5)
Total	40

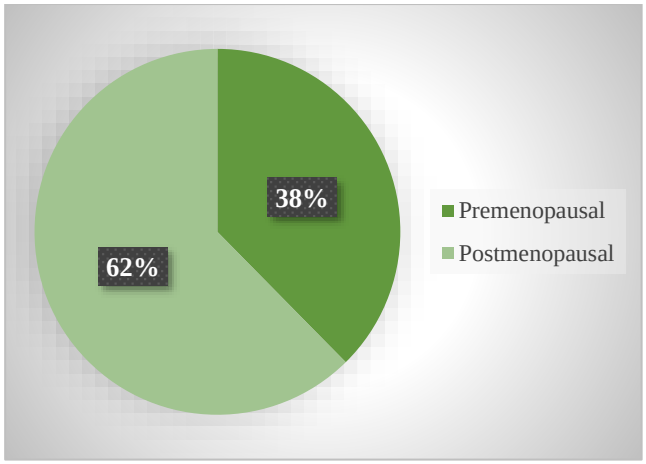

Figure 1: Distribution of cases according to gonadal activity.

Table 2: Distribution of cases according to stage of tumor at primary visit at hospital, (n=40).

Tumor staging	Frequency (%)
T2	11 (27.5)
T3	23 (57.5)
T4	6 (15)
Nodal staging	
N0	3 (7.5)
N1	25 (62.5)
N2	12 (30)

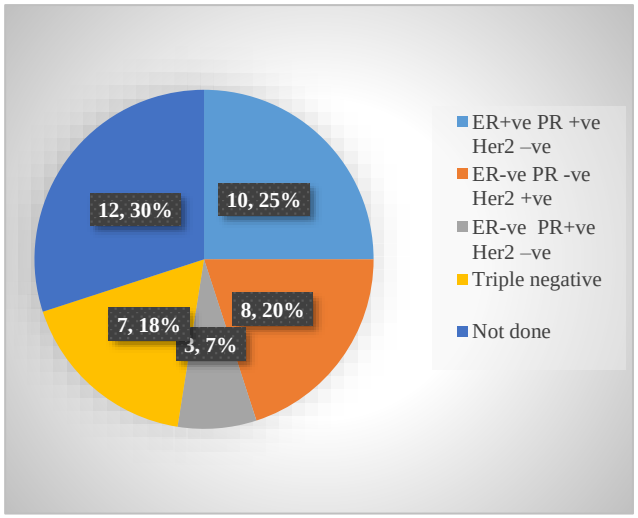

Figure 2: Distribution of Receptor status among study participants, (n=40).

Table 3: Distribution of response to chemotherapy among cases, (n=40).

Response	Frequency (%)
Complete response	4 (10)
Partial response	33 (82.5)
No response	3 (7.5)
Total	40

DISCUSSION

Management of LABC requires multimodality approach involving oncophysician, oncosurgeon and radiation oncologist.[6-8] Patients with locally advanced disease encompass a wide range of clinical scenarios including advanced primary tumors (stage 3), advanced nodal disease (fixed axillary nodes or involvement of ipsilateral supraclavicular, infraclavicular or internal mammary nodes) and inflammatory carcinomas. The prognosis of women with locally advanced breast tumors depends on age, tumor size, grade of tumor and extent of lymph node involvement

Maximum number of cases with LABC belongs to age group between 35-54 years. Considering the literature with maximum incidence of carcinoma breast in Indian women belongs to the age group of 40-50 years. So, with this age group maximum patients were of perimenopausal period. The mean age was 45 which is comparable with 46-50 years in studies of the Tapesh et al, and Deo et al.[9,10] In the present study maximum cases 56.6% belong to tumor size-T3, while T2 and T4 were in 26.6% and 16.6% of cases respectively. Tapesh et al reported 4.7%, 37.9% and 57.5% of cases in sizes of T2, T3 and T4 respectively.[9] In another study conducted by Deo et al, 8%, 76% and 16% cases were belonged to T2, T3 and T4 sizes respectively.[9,10] Patients with larger cancers have poorer survival rates. Hormone receptor positivity is associated with a longer survival time. ER, PR and HER 2 neu positive patients have better survival then triple negative (ER, PR and HER 2 neu), as in receptor positive tumors response to chemotherapeutic regimens predictively.

The treatment of LABC requires a combination of systemic chemotherapy, surgery and radiotherapy to optimize the chance of cure. The earliest therapy for LABC was radical mastectomy. However, patients with supraclavicular involvement, edema of the arm, satellite skin nodules and extensive breast edema were considered markers of inoperable disease. Patients who were treated with primary radiotherapy also had a high risk for disease recurrence and death, as well as the complications of chest wall fibrosis, lymphedema, skin ulceration and skin necrosis. Neoadjuvant chemotherapy is the standard treatment for women who have tumors that are too large to remove surgically with a cosmetically acceptable outcome. It is also the standard treatment for women with inflammatory breast cancer. Successful neoadjuvant chemotherapy will shrink the tumor before surgery, making it easier to remove. This treatment will also decrease the chances of recurrence. For a small number of women, having neoadjuvant chemotherapy may allow them to have breast conserving surgery, such as lumpectomy, rather than a mastectomy.

Many standard chemotherapy regimens exist for the adjuvant and neoadjuvant treatments of breast cancer. According to the early breast cancer trialists' group

(EBCTG), as neoadjuvant therapy, anthracycline-based chemotherapy regimens has been proven to be superior for LABC while for patients with node positive LABC, the addition of a taxane to an anthracycline-based regimen improves overall survival. For women with HER-2 positive metastatic breast cancer, treatment with transtuzumab in combination with chemotherapy can improve survival.

In present study about 93% of cases responded to neoadjuvant chemotherapy with 10% of cases shows complete clinical response where tumor becomes completely free from skin or pectoral muscles or negative axillary lymph nodes. While response was seen in 83.3% and 66% cases in study conducted by Tapesh et al and Deo et al respectively.[9,10] Complete pathological response was seen in 13.3% while it was 16.6% in case of study conducted by Tapesh et al.[9] After patients complete neoadjuvant chemotherapy. They should proceed with definitive local therapy. The traditional approach has been to treat women with locally advanced tumors with modified radical mastectomy.

All patients were subjected to modified radical mastectomy after 4 cycles of neo adjuvant chemotherapy except 02 patients presented with local sepsis were subjected to toilet mastectomy followed by adjuvant chemotherapy, radiotherapy and hormonal therapy. There was no mortality in patients subjected to neoadjuvant therapy, but one mortality and one recurrence in patients with adjuvant therapy in LABC comparable to available studies in literature. In the view of review of literature, a study conducted at Stanford University observed 73% of women with T4 (inflammatory or locally advanced) carcinomas shows clinical response to neoadjuvant chemotherapy. They also come out with the secondary effect of neoadjuvant chemotherapy was possibility of lumpectomy and radiation rather than mastectomy in cases that respond dramatically.

Limitation

It is hospital-based study so, small sample size for study was taken. Therefore, the results of study will not be generalized. Also, there was Difference in age group, Staging and Metastasis status of all patients were variant, and so Outcomes were altered.

CONCLUSION

With the evidence from the literature and study conducted earlier, our observations of clinical response of neoadjuvant chemotherapy in patients with LABC had corroborative evidence. Overall observations suggested that most of the LABC responds to neoadjuvant chemotherapy with minimum post-operative morbidity and mortality.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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