

# Assessment of Clinical Response to Multimodality Approach in Advanced Carcinoma Breast

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## ABSTRACT

**Background:** Cases of carcinoma breast with TNM stage 3 are considered as locally advanced breast cancer. This study was done to demonstrate the effect of multimodal treatment approach in cases of stage 3 technically inoperable breast cancer. Its effect on clinical response was studied. **Methods:** This prospective study was carried out in department of general surgery, government Medical College, Amritsar, Punjab. Main part of multimodal approach is neoadjuvant chemotherapy, so in collaboration with department of radiotherapy, relevant data was collected. 25 cases of locally advanced breast carcinoma were studied. These patients were studied on treatment with FAC regimen (as neoadjuvant chemotherapy), then underwent surgical excision (MRM) followed by chemotherapy, radiotherapy and hormonal therapy wherever indicated, and response was assessed. **Results:** Initially assessment of lump was done after 3 cycle of chemotherapy. 2 patients (8%) have reduction <50%, 22 patients (88%) have reduction in size which ranges between 51-75% of the initial, remaining 1 patient (4%) has reduction >75% of the initial. Thus making them operable therefore after this they all had undergone modified radical mastectomy. During follow up period no lump was detected clinically, ultrasonographically or radiologically. There was no any loco-regional recurrence in any case. **Conclusion:** The study demonstrated the effectiveness of neoadjuvant chemotherapy in down staging the tumor enabling definitive surgery with less morbidity.

**Keywords:** Locally advanced breast cancer (LABC), FAC regimen, Chemotherapy, Surgery.

## INTRODUCTION

Breast cancer is the most common site specific cancer among women worldwide. It accounts for about 33% of the female cancer. Carcinoma breast disease is about 100 times more common among women than men.<sup>[1]</sup> Risk of developing breast cancer increases as age advances. About 1 out of 8 invasive breast cancers are found in women younger than 45, while about 2 out of 3 invasive breast cancers are found in women of age group 55 years or older.<sup>[2]</sup> About 5% to 10% of breast cancer cases are thought to be hereditary, meaning that they result directly from gene defects BRCA1 and BRCA2. The most common cause of hereditary breast cancer is an inherited mutation in the BRCA1 and BRCA2 genes families with BRCA1 mutations the lifetime risk of breast cancer on average seems to be in the range of 55 to 65%.<sup>[3]</sup> For BRCA2 mutations the risk is lower, around 45%. Breast cancers linked to these mutations occur more often in younger women.<sup>[3]</sup>

Despite an increasing incidence, mortality from breast cancer continue to fall may be due to earlier detection via mammography/ USG and better treatment approach. In India it is second most common cancer after cancer of uterine cervix. Studies suggest that breast feeding may slightly lower breast cancer risk, especially if it is continued for 1½ to 2 years.<sup>[4]</sup>

Life style is important for genesis of breast cancer. Obesity is an important risk factor for development of breast cancer. Renehan et al<sup>5</sup> estimated that for each 5 kg/m<sup>2</sup> increase in BMI (body mass index), the risk of breast cancer was increased by 12%.<sup>[5]</sup> In our study out of 25 cases, 5 patients, are obese, that is 20% of the patients in the study are obese. Several studies, important is Rostov et al,<sup>[6]</sup> has found strong correlation between metabolic syndrome, obesity and development of breast cancer.<sup>[6]</sup>

The age of menarche and age of first child birth is to identify the duration of menstrual cycles between these two time periods which when increases, causes the significant risk for development of breast cancer as per Gajalakshmi and Shanta.<sup>[7]</sup> The risk is significant when the duration of menstrual cycles is more than 12 years. Although there are only three patients, with age less than average age of menarche

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and there are only five patients with age higher than average age at first pregnancy. Despite this figure, in my overall study, there are total 8 females having the duration of menstrual cycles more than 12. Early age of menarche and higher age at first child birth are not an independent risk for breast cancer, but the significant difference between the two is risk factor for development of breast cancer.

Breast feeding has an important role in incidence of breast cancer. According to the article published in lancet "Breast cancer and breast feeding".<sup>8</sup> In our study, out of 25 women with cancer, there are total 4 women who have duration of breast feeding <6 months, including 2 women who are nulliparous, so, it comes out to be, 16% women have less duration of breast feeding history including 2 women who are nulliparous.

Use of hormonal replacement therapy (HRT) is an important risk factor for development of breast cancer. Collaborative group on hormonal factor in breast cancer has brought together and reanalyzed about 90% of the worldwide epidemiological incidence on the relation between risk of breast cancer and use of hormone replacement therapy (HRT). Data from on 52,705 women with breast cancer and 108411 women without breast cancer was collected, checked and analysed carefully.<sup>[9]</sup>

The main analysis are based on 53,865 postmenopausal women with a known age at menopause, among them, 17830 (33%) had used HRT at some time.<sup>9</sup> The median age at first use was 48 Years and 34% of ever-user had used HRT for 5 years or longer. Among current users of HRT or those who used 1-4 years previously, the relative risk of having breast cancer diagnosed increased by a factor 1.023 for each year of use, the relative risk was 1.35 for women who had used HRT for 5 years or longer.<sup>[9]</sup> This increase is comparable with effect on breast cancer of delaying menopause, among never uses of HRT the relative risk increases by a factor of 1.028, for each year older at menopause. 5 year or more after cessation of HRT use, there was no significant risk of HRT on breast cancer.<sup>[9]</sup>

Thus, the risk of having breast cancer diagnosed is increased in women using HRT and increases with increasing duration of use. The effect is reduced after cessation of use of HRT and has largely, if not wholly, disappeared after about 5 years. In our study, there are 3 patients with use of HRT, one patient of age 47 years, who had her menopause at the age of 45 years, is currently on HRT. Other one, of age 56 years is also on HRT at the time of development of breast cancer. She had her menopause at the age of 46 years. She has been using HRT for last 3 years. 3rd patient of 67 years has left HRT 4 years back, having her menopause at 45 years of age, although she had left HRT 4 year back, despite thus she must had some association of breast cancer and HRT use. She had used HRT for 4 years continuously. Therefore it will be correct to say, according to the

studies that there is some definite relationship between the use of hormone replacement therapy and development of breast cancer.

Locally advanced breast cancer refer to stage 3 disease which includes T3 tumor with N1, N2 or N3 disease, T4 tumor with any N classification, or any T classification with N2 or N2 regional lymph node involvement.<sup>[10]</sup> There should not be evidence of distant metastasis (M1).

## MATERIALS AND METHODS

This prospective study was done in a department of General Surgery, Govt. Medical College, Amritsar, Punjab. This study was done to assess the clinical response of the patient to multimodal treatment approach for breast cancer. Patients with evidence of distant metastasis and patients who had received chemotherapeutic regimen other than FAC (5-FU, Adriamycin and cyclophosphamide) were excluded. The diagnosis of breast cancer was made cytologically by FNAC. All the 25 patients were started on FAC regime given on day 1 and repeated 3 weeks for 3 cycles.

After neoadjuvant chemotherapy, all the patients were scheduled for modified radical mastectomy and the specimen subjected to histopathological examination. All the patients were scheduled for post-operative chemotherapy of FAC regime for 3 cycles. Further radiotherapy to chest wall axilla and supraclavicular area. Finally patients were prescribed Tab. Tamoxifen 20mgs per day for 5 years, wherever indicated. Patients were followed up after 3 months and 6 months.

## RESULTS

The size was assessed clinically by comparing it with maximum dimension of the lump before the chemotherapy. 2 patients (8%) have reduction less than 50% in the products of the two maximum perpendicular diameter, 22 patients ((88%) have reduction ranging between 51-75% in the products of the two maximum perpendicular diameter, whereas remaining 1 patient (4%) has reduction greater than 75% in the product of the two maximum perpendicular diameters.

No patients developed recurrence in the same breast or any lump in the opposite breast on clinical examination. There was no any metastasis seen in abdomen on USG and in chest on X- Ray during follow up period. All the patients well tolerated the treatment and are clinically in good health.

### Pre and post chemotherapy tumor size

No. of Patients	Percentage reduction in size of the lump (in the products of two maximum perpendicular diameter)
2	<50%
22	51-75%
1	>75%

## DISCUSSION

Locally advanced breast cancer, LABC refer to tumor size more than 5cm (T3) or tumor fixed to chest wall or presence of skin ulceration, satellite nodule or peau d' orange or regional lymph nodes, but without evidence of metastasis (M0).

Neoadjuvant chemotherapy has a great role in locally advanced breast cancer as it converts inoperable breast cancer to operable cancer, thus causing the down staging of the tumor. Neo adjuvant systemic therapy integrated into a multimodality program is the established treatment in LABC.<sup>[11,12]</sup> In Milan trial,<sup>13</sup> the best results were achieved when surgery was done after neoadjuvant chemotherapy, with 82% locoregional control and 25% 6 year disease free survival.

The study conducted by G.N. Hartobagyi et al,<sup>[14]</sup> 52 patients with locally advanced breast cancer without distant metastasis were treated with FAC regime, followed by surgery, chemotherapy and radiotherapy. 49 out of 52 patients were rendered free of clinically detectable disease. The median disease free interval was 24 months.

Another similar study conducted by Gopal A et al,<sup>[15]</sup> reported that 20% of the patients had complete clinical response at the completion of 3 cycles of chemotherapy with FAC regime. 48% had partial response. In 32% patients, stasis was observed. None showed increase in tumor size during treatment.

The reduction in size of the tumor and it becoming more mobile and less fixed to skin obviates the need for skin grafting or complex reconstruction.

Usually 3 cycles of neoadjuvant chemotherapy is generally accepted as standard before surgery. In our study none of the patients showed disease progression during the therapy. So the multimodal treatment approach is the best suited treatment for locally advanced breast cancer. Combination of surgery with chemo-radio-hormonal therapy yielded superior loco regional control.

## CONCLUSION

The study clearly showed the effectiveness of neoadjuvant therapy in down staging the tumor, thus converting inoperable tumor to the operable one, due to which definitive surgery can be done with less morbidity and good results. In our study 2 patients have reduction <50%, 22 have reduction, 51-75% whereas 1 patient have reduction >75% of their pre chemotherapeutic size. As size decrease after neoadjuvant chemotherapy, thus surgical results are good and disease free survival rate also increase, with better loco-regional control.

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