



A CLINICAL EVALUATION OF RESPONSE TO NEO-ADJUVANT CHEMOTHERAPY IN BREAST MALIGNANCIES.

General Surgery

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ABSTRACT

INTRODUCTION: Chemotherapy in breast cancer treatment has assumed a greater significance ever since researchers have given breast cancer the status of systemic disease. Surgery can eradicate only the local disease, and eradication of the systemic component involves the use of chemotherapeutic agents.

MATERIALS AND METHODS: This study involved the study of 50 patients with stage III disease admitted at Alluri Sitarama Raju Academy of Medical Sciences Hospital, Dept of General Surgery between November 2019 to April 2021.

This is a prospective cohort study involves patients who fall in stage III (LABC) locally advanced breast carcinoma were considered for the study and received Neoadjuvant Chemotherapy (AC regimen).

RESULTS: In the present study the mean tumour size in centimeter before treatment was 7.83 ± 1.04 and after treatment it was 2.60 ± 0.97 . There was a statistically significant difference observed between the mean size of tumour in centimeter before and after chemotherapy as the p value calculated to be less than 0.05.

CONCLUSION: Patients with stage III Breast Cancer will benefit from tumour down staging. Neo- adjuvant chemotherapy is preferred for down staging the tumor and lymph nodes.

KEYWORDS

breast carcinoma, neo adjuvant chemotherapy .

INTRODUCTION:

Carcinoma of the breast from the very beginning has been a feared disease. Till today, there is an aura of fear that surrounds the mention of this name 'breast cancer.'

Medical research and efforts by various groups and individuals have given many treatment modalities, each of which is incomplete and has to be supplemented by another.

Among all treatment modalities, surgery has come to be accepted as the 'golden standard,' to which all other treatment modalities have to be compared. Halsted's radical mastectomy has been accepted as the main factor for comparison of results of any form of treatment; that is, the results of treatment of breast cancer by any modality or a combination of modalities have to be compared to results obtained by Halsted with his radical mastectomy.

Other treatment modalities such as chemotherapy and radiotherapy are considered adjuvant to surgery and are incomplete by themselves. Chemotherapy in breast cancer treatment has assumed a greater significance ever since researchers have given breast cancer the status of systemic disease. Surgery can eradicate only the local disease, and eradication of the systemic component involves the use of chemotherapeutic agents.

Chemotherapy may be given as an adjuvant postoperatively or Neo-adjuvant chemotherapy, where two to three doses are given prior to surgery, followed by the remaining cycles post-operatively. Occasionally in very advanced cases, chemotherapy alone may be given as a palliative measure when any form of surgery is likely to result in an extensive deformity that will compromise on the quality of life without a significant increase in life span.

This study deals with the administration of Neo-adjuvant chemotherapy in patients who have been worked up for surgery. All patients were given three cycles of a chemotherapeutic regimen as per recommended doses, and the effect was studied three weeks after the third cycle, just before surgery.

AIMS AND OBJECTIVES:

To evaluate and quantify the response to neoadjuvant chemotherapy by physical examination and imaging modalities.

- To define a group of suitable subjects in whom neoadjuvant chemotherapy is likely to be beneficial.
- Reduction in size of the primary tumor.
- Effect on lymph node status.
- Change in the clinical stage of the tumor after anterior chemotherapy.

MATERIALS AND METHODS:

This study involved the study of 50 patients with stage III disease admitted Alluri Sitarama Raju Academy of Medical Sciences Hospital, Dept of General Surgery.

This is a prospective cohort study from November 2019 to April 2021.

All patients admitted with breast cancer underwent a detailed assessment. Clinical staging of the disease was done (TNM Staging).

Those patients who fall in stage III (LABC) locally advanced breast carcinoma were considered for the study and received Neoadjuvant chemotherapy (AC regimen).

FNAC/Biopsy of breast lump did confirmation of diagnosis.

Accurate measurement of breast lump was done in each patient; the dimensions were marked on a simple line diagram with reference to the quadrant involved and size of the lump compared before and after neoadjuvant chemotherapy sono-mammogram.

Size and number, and fixity of affected lymph nodes were also recorded before and after chemotherapy.

Each patient received three cycles of chemotherapy consisting of cyclophosphamide and adriamycin, doses calculated according to body surface area, with three weeks interval between each cycle.

Patients were evaluated three weeks after the 3rd cycle of chemotherapy.

Clinical staging is repeated, and all factors such as tumor size, lymph node status.

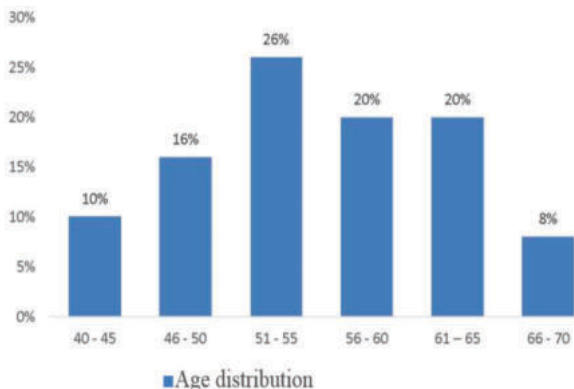
Compared with recordings taken before chemotherapy. The data thus

collected was then analyzed, significance determined, and the literature on the topic was reviewed.

Each study parameter designed in proforma was compared pre and post chemotherapy in those included in the study. Percentages of various parameters were calculated comparing prechemotherapy with post-chemotherapy after assessing different parameters as in proforma.

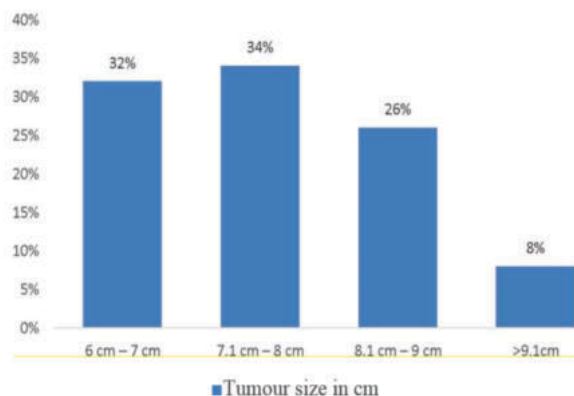
RESULTS:

Graph 1: Age distribution

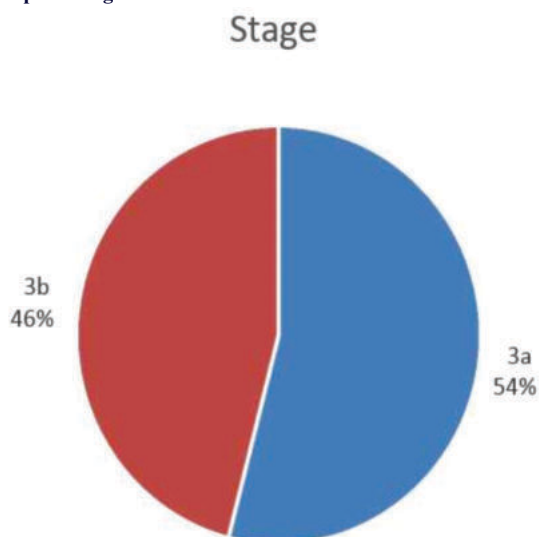


In the present study, the mean age was 55.02 ± 7.30 . Majority of the study participants belonged to 51-55 years age group.

Graph 2: Tumour size in cm

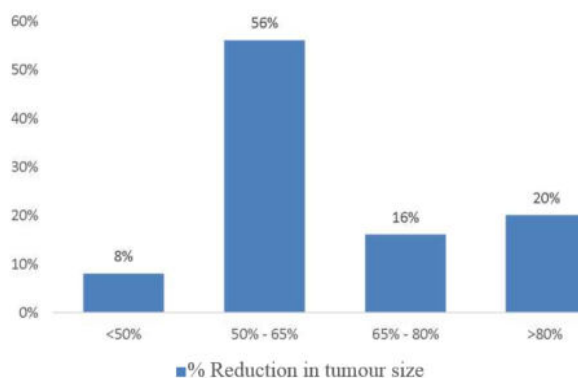


Graph 3: stage



54% were diagnosed to have stage 3a cancer and 46% diagnosed as stage 3b cancer

Graph 4: percentage of tumour size reduction



In the present study, mean reduction in tumor size after chemotherapy was 66.50 ± 12.42 . Majority i.e. 56% had 50% - 65% reduction of the tumour size.

Table 1

Stage after 3rd Chemotherapy	Frequency, n(%)
I	2 (4%)
II	48 (96%)
Total	50 (100%)

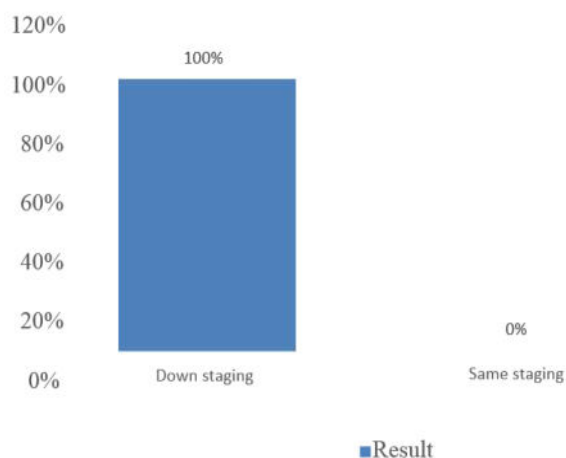
In the present study, after chemotherapy 96% diagnosed as stage II and 4% diagnosed as stage I.

Table 2: Stage after 3rd Chemotherapy

Result	Frequency, n(%)
Down staging	50 (100%)
Same staging	0 (0%)
Total	50 (100%)

All the study participants i.e. 100% had down staging after chemotherapy.

Graph 5: Result



% Reduction in tumour size	Frequency, n (%)	IIIa	IIIb
<50%	4 (8%)	3 (6%)	1 (2%)
50% - 65%	28 (56%)	10 (20%)	18 (36%)
65% - 80%	8 (16%)	4 (8%)	4 (8%)
>80%	10 (20%)	10 (20%)	0 (0%)
Total	50 (100%)	27 (54%)	23 (46%)

Chi-square value : 13 , P value = 0.005* (statistically significant)

In the present study, after chemotherapy majority i.e. 56% had 50% - 65% reduction in tumour size. And 20% had >80% reduction in tumour size.

Among the IIIa group, <50% reduction observed in 6% of the study participants, 50-65% reduction in 20% of the participants, 65% - 80% reduction 8% of participants, >80% reduction in 20% of the participants.

Among IIb group, <50% reduction observed in 2% of the study participants, 50-65% reduction in 36% of the participants, 65% - 80% reduction 8% of participants.

This observation was found to be statistically significant as the p value calculated to be <0.05.

DISCUSSION:

This dissertation deals with the study of breast cancer patients who were admitted at Alluri Sitarama Raju Academy of Medical Sciences Hospital and received anterior chemotherapy.

A total of 50 patients who presented in stage III were included in the study during the period November 2019 to April 2021.

Most common stage at presentation in Indian population is stage III¹. In our study we have included only the patients who have presented with stage III.

Fifty patients with locally advanced breast cancer received three cycles of Neo-adjuvant chemotherapy with cyclophosphamide and Adriamycin.

All the patients treated in this manner were seen to show a good response to chemotherapy. Out of 30 patients who received Neo-adjuvant chemotherapy with AC, 76.6% underwent downstaging of the tumor by one or more stages. Results of NSABP B-18 (National Surgical Adjuvant Breast Project) on the effect of preoperative chemotherapy on tumor response indicate that following administration of preoperative chemotherapy, 36% of patients obtained a complete clinical response and 43% of patients obtained a partial clinical response, for an overall response rate of 79%^{2,3}. These patients were closely monitored to effect these drugs on the tumour, lymph nodes, and other metastasis.

All patients in this study had a clinically palpable tumor. All the tumors have responded to anterior chemotherapy with a decrease in size. Resistance to chemotherapy was not encountered in the course of the study. No patient showed complete clinical resolution. In NSABP B-18 trials, 13% of the patients achieved a pathologic complete response (absence of invasive tumor in the breast specimen following neoadjuvant chemotherapy)^{2,3,4}.

Tumour size in Cm: The main tumour size in centimetres in present study was 7.83 ± 1.04 . 32% had a tumour size of 6 - 7 centimetres and 34% had a tumour size of 7.1 - 8 centimetre, 26% had a tumor size of 8.1 - 9 centimeters, 8% had a tumour size of > 9.1 centimeter

Jadhav et al⁵ in their study reported that 84.38% patients had lump size between 5-7.5 cm. Average of the maximum dimension of the lump was 6.3 cm.

Stage: Majority i.e. 54% were diagnosed to have 3a stage cancer and 46% had stage 3b cancer in the present study.

In a study conducted by **Gedam et al⁶**, clinical presentation and management of locally advanced breast carcinoma majority of patients were in stage IIIA (55.6%) followed by stage IIIB (37.7%).

Percentage of tumour size reduction: The mean percentage of tumour size reduction in the present study was 66.50 ± 12.42 . 56% of the study participants had a tumour size reduction of 50% to 65%.

20% had a tumour size reduction of > 80% , 16% had a tumour size reduction of 65 To 80% and 8% had a tumour size reduction of less than 50%.

Stage after 3rd Chemotherapy

After the 3rd chemotherapy, 96% of the study participants were diagnosed as stage 2 whereas it was diagnosed to be stage one in 4% of the study participants. Down staging was observed in all the study participants after 3rd chemotherapy.

In **Narendra et al⁷** study On pre-surgery evaluation, 93% of the patients had down staging of the disease of which 29% had complete remission and 64% had partial response. Among the partial responders, 12% had only mammosonographic evidence of the residual disease. Two patients had developed systemic metastasis.

Totally 48 patients (57%) underwent modified radical mastectomy and breast could be conserved in the remaining 36 patients (43%). Totally 31 patients (36%, $P = 0.027$) achieved pCR. At the beginning of the study clinically 82 patients were T4/T3, N + or any T with N2/N3 disease and after NACT only 26 patients had persistent T3/T4 or N2/N3 disease, thus 75% of the patients were down staged [Figure 2]. Of the 73 node positive patients, 47 (64%) became node negative following NACT.

A potential benefit of NAC is that tumour response may be assessed in vivo by measuring tumour size at regular intervals. Ineffective chemotherapy can be stopped, avoiding unnecessary toxicity¹⁰.

Correlation with size reduction in % with stage

In the present study, after chemotherapy majority i.e. 56% had 50% - 65% reduction in tumour size. And 20% had >80% reduction in tumour size.

Among the IIIa group, <50% reduction observed in 6% of the study participants, 50-65% reduction in 20% of the participants, 65% - 80% reduction 8% of participants, >80% reduction in 20% of the participants.

Among IIb group, <50% reduction observed in 2% of the study participants, 50-65% reduction in 36% of the participants, 65% - 80% reduction 8% of participants.

This observation was found to be statistically significant as the p value calculated to be <0.05.

Mean size of tumor in cm before and after chemotherapy

In the present study the mean tumour size in centimeter before treatment was 7.83 ± 1.04 and after treatment it was 2.60 ± 0.97

There was a statistically significant difference observed between the mean size of tumour in centimetre before and after chemotherapy as the p value calculated to be less than 0.05.

Subhashree Chandrashekaran et al⁸ in their study reported that Chemotherapy regimen lasted for 63 days with FAC regimen. Follow up MRI was done in the range of 12 to 18 days following completion of third cycle of chemotherapy. The interval between follow up MRI and surgery was 7 to 14 days. 15 out of 20 patients showed a partial response (75%) in MRI as assessed by longest tumor diameter and morphologic tumor volume. 3 out of 20 patients were morphologic complete responders (15%) as evidenced by no demonstrable mass in follow up MRI. Two out of 20 patients had stable disease (10%).

CONCLUSION:

Patients with stage III Breast Cancer will benefit from tumour down staging. Neo- adjuvant chemotherapy is preferred for down staging the tumor and lymph nodes. Delaying the surgery while systemic therapy is being delivered does not upstage the disease. Tumor response to neo-adjuvant chemotherapy is more compared to the lymph nodal response. Benefit from tumor downstaging can be achieved by Neo-adjuvant chemotherapy and it is the preferred approach for patients with bulky and locally advanced disease at the time of diagnosis

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