



A PROSPECTIVE OBSERVATIONAL STUDY OF RESPONSE TO NEOADJUVANT CHEMOTHERAPY IN LOCALLY ADVANCED BREAST CANCER IN TERTIARY CENTRE

Manojit Sarkar

3RD Year Pgt,dept of General Surgery,nrsmch,kolkata,west Bengal

Asis Kumar Saha*

Associate Professor,dept of General Surgery,nrsmch,kolkata*Corresponding Author

ABSTRACT 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'. Neoadjuvant chemotherapy (NAC) is increasingly used to treat patients with locally advanced breast cancer (LABC). Such regimens can increase rates of breast-conserving therapy (BCT) compared with post-operative chemotherapy² and may minimize the need for aggressive nodal surgery with axillary lymph node dissection. **Aims:** To assess the change of clinical staging after Neoadjuvant Chemotherapy, Assessment of Lymph node status after neoadjuvant Chemotherapy and type of surgery suitable after Neoadjuvant Chemotherapy. **Materials and method:** The present study was a hospital based observational study. The study conducted in Nil Ratan Sircar Medical College & Hospital. The study duration was One year (June 2021 to May 2022). 50 patients were included in this study. **Result:** In our study, all patients [50 (100.0%)] had Lymph node involvement. We showed that, most of the patients had Stage IIIA [25 (50.0%)]. However, Stage IIIB [15 (32.0%)] followed by Stage IIIC [10 (20.0%)] which was statistically significant ($p=.00168$). It was found that, all patients [50 (100.0%)] had Anterior Chemotherapy. Our study showed that, most of the patients had Stage IIB after chemotherapy [22 (44.0%)] and it was statistically not significant ($p<.14706$) ($z=1.4499$). In our study, higher number of patients had Down stage Result [35 (70.0%)] followed by Same Result [15 (30.0%)] but this was statistically significant ($p=.00006$) ($z=4$). We showed that, the mean Tumor size of patients was $[7.2880 \pm 1.4822 \text{ (cm)}]$ and mean % of size reduction of patients was $[58.0000 \pm 15.0509]$. **Conclusion:** we conclude that, the change of clinical staging after Neoadjuvant Chemotherapy, Lymph node status after neoadjuvant Chemotherapy.

KEYWORDS : Neoadjuvant chemotherapy (NAC), Lymph node status and Breast Cancer.

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 has given number of modalities of treatment of breast cancer, each of which are incomplete in themselves, and have to be supplemented by another.

Among all modalities of treatment, surgery has come to be accepted as the 'golden standard', to which all other modalities of treatment 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 lasted with his radical mastectomy.

Other modalities of treatment such as chemotherapy and radiotherapy are considered as adjuvant to surgery and are incomplete by themselves. Chemotherapy in the treatment of breast cancer has assumed a greater significance ever since researchers have given breast cancer the status of a systemic disease. Surgery as such 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 post operatively, or as 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 extensive deformity that will compromise on quality of life without a significant increase in life span. With the suggestion that the behaviour of a breast cancer is often the expression of systemic disease present at the time of diagnosis, surgical management of local disease has become more conservative.

This dissertation deals with the administration of Neo-adjuvant chemotherapy in patients who have been worked up for surgery. All patients were given four cycles of a chemotherapeutic regimen as per recommended doses, and the effect was studied three weeks after the 4th cycle, just prior to surgery. However, the long term follow up of patients and a formal comparison of the 5 - year survival rates and recurrence/metastasis between Neo-adjuvant and routine post-operative chemotherapy was out of the scope of this dissertation. Neoadjuvant chemotherapy (NAC) is increasingly used to treat patients with locally advanced breast cancer (LABC)^{1,2,3}. Such regimens can increase rates of breast-conserving therapy (BCT) compared with post-operative chemotherapy² and may minimize the need for aggressive nodal surgery with axillary lymph node dissection

^{4,5}. Other purported advantages include in vivo tumour response assessment and prognostication based on degree of response. Patients with HER2-receptor positive or triple-negative disease may also benefit from early treatment of distant micrometastases due to increased metastatic potential of these disease types^{6,7}. Despite these potential advantages, NAC has not demonstrated improved survival over adjuvant chemotherapy in randomized trials.

The NSABP B-18 and B-27 trials delivered anthracycline-based NAC (and included taxanes in B-27). Patients who underwent breast conserving surgery (BCS) after NAC received whole breast radiation therapy (RT) alone, while mastectomy patients did not receive RT. These trials demonstrated locoregional recurrence rates of 12.3% for mastectomy patients and 10.3% for BCS patients⁸; overall survival (OS) rates were 75% at 8 years⁶. Subsequent retrospective studies^{9,10} have suggested that adjuvant RT decreases the rate of locoregional recurrence (LRR) and improves survival after NAC and surgery, but this has not been evaluated with randomized trials. Given the absence of level I evidence, routine practice at their centre is to offer radiation therapy after NAC and surgery.

MATERIALS AND METHODS

STUDY AREA: Department of General Surgery, Nil Ratan Sircar Medical College & Hospital

STUDY POPULATION: Patient diagnosed as a case of Carcinoma breast by FNAC/Trucut biopsy

STUDY PERIOD: January 2021 to June 2022

SAMPLE SIZE: 50(All cases admitted with Locally advanced Carcinoma breast(from 1st January 2021 to 31st December 2021) was included in this study. In 2020 a total number of 46 cases were admitted with Locally advanced Carcinoma breast IN General surgery department. So, I have taken a sample size of 50.)

STUDY DESIGN: Prospective Observational Study

MATERIAL AND METHODS:

This dissertation involved the study of 50 patients with locally advanced breast cancer who were admitted at Nil Ratan Sircar Medical College, Dept of surgery.

This is a Prospective Observational study from 1st January 2021 to 31st December 2021 will be included in this study. All patients admitted with breast cancer underwent a detailed assessment. Clinical staging of the disease was done (TNM Staging).(AJCC 8th

Edition) Those patients who fall in locally advanced breast carcinoma were considered for study and received 4 cycles Neoadjuvant chemotherapy (AC regimen). Confirmation of diagnosis was done by FNAC/core cut Biopsy of breast lump. Accurate measurement of breast lump was done in each patient, compared before and after neoadjuvant chemotherapy clinically & with Vernier callipers and number and fixity of affected lymph nodes was also recorded before and after chemotherapy. Each patient received 4 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 3 weeks after 4 cycle of chemotherapy. Clinical staging repeated and all factors such as tumour size, lymph node status, & staging after chemotherapy. The data thus collected was then analysed, significance determined and the literature available on the topic was reviewed.

STUDY AREA: Selected from outdoor of Department of General surgery, diagnosed as locally advanced carcinoma breast.

INCLUSION CRITERIA: Female breast Cancer Stage IIB (except T2N1M0) - Stage III

EXCLUSION CRITERIA:

1. Benign breast lump
2. Male breast carcinoma
3. Female <18 years
4. Metastatic breast carcinoma
5. Patients under other clinical trials
6. Associated comorbidities that may prevent proper chemotherapy
7. Patients not willing to undergo this study.

DISCUSSION

A Prospective Study was conducted in Department of General Surgery, NRSMC & H. The study period was January 2021 to June 2022. 50 patients were included in this study.

Choudhary P et al¹¹ (2020) found that the data regarding incidence, response rates to neoadjuvant chemotherapy (NACT) and factors affecting pathological complete response (pCR) rate in locally advanced breast cancer (LABC) patients are lacking from India. The median age of diagnosis was 46 years (range 24-72 years).

Kunnuru SK et al¹² (2020) found that to assess the effectiveness of neoadjuvant chemotherapy and its impact on the clinical and pathological response in locally advanced breast cancer. The median age of the patients at the time of diagnosis was 44 years (range=24-73).

In our study, out of 50 patients, most of the patients were 51-60 years of age [20 (40.0%)] rest of 15 (30.0%) patients were 41-50 years of age, 10 (20.0%) patients were ≤40 years of age and 5 (10.0%) patients were >61 years of age. Age was statistically significant ($p=0.0054$) ($z=3.4641$). The mean Age of patients was $[49.9600 \pm 9.5404]$.

In our study, all patients [50 (100.0%)] had Lymph node involvement. We found that, most of the patients had tumor in size 5-7 cm [30 (60.0%)] followed by Tumor in size 8-10 cm [30 (60.0%)] but this was statistically significant ($p=0.455$).

Bhattacharyya T et al¹³ (2014) observed that neoadjuvant chemotherapy (NACT) has dramatically changed the management of locally advanced breast cancer (LABC). A while 28 (18.9%) patients developed distant metastasis.

El-Mahdy MM et al¹⁴ (2020) found that presence of TILs in breast cancer indicates better therapeutic responses to neoadjuvant chemotherapy (NAC), increased pCR and improved outcome. Distant metastasis ($p=0.025$).

In our study, all patients had no distant metastasis [50 (100.0%)].

Klein J et al¹⁵ (2019) examined that Neoadjuvant chemotherapy (NAC) is increasingly used to treat locally advanced breast cancer (LABC). The cohort included 103 patients nearly equally divided between Stage II ($n=53$) and Stage III ($n=50$). Stage group ($p=0.05$).

We showed that, most of the patients had Stage IIIA [25 (50.0%)]. However, Stage IIIB [15 (32.0%)] followed by Stage IIIC [10 (20.0%)] which was statistically significant ($p=0.0168$).

It was found that, all patients [50 (100.0%)] had Anterior Chemotherapy.

Tang S et al¹⁶ (2020) showed that this retrospective analysis was designed to research whether clinical response partial response (PR)/complete response (CR) and pathological response (PCR) to neoadjuvant chemotherapy can translate into prognosis benefit pathological response in patients with locally advanced breast cancer and whether different chemotherapy regimens will influence the outcomes. Clinical response was strongly correlated with lymph nodes status ($P=0.032$).

Gogia A et al¹⁷ (2014) showed that this study was to assess the response rates (clinical and pathological) with docetaxel and epirubicin combination chemotherapy and its effect on outcome. 90% had clinically palpable lymph nodes at diagnosis.

Our study showed that, Same Lymph node status [27 (54.0%)] was higher than down stage Lymph node status [23 (46.0%)] but this was not statistically significant ($p=0.42372$) ($z=8$).

We found that, more number of patients had Size reduction 25-50% [20 (40.0%)] rest of 50-75% [15 (30.0%)], >75-99% [10 (20.0%)] and <25% [5 (10.0%)] though it was statistically significant ($p=0.00054$) ($z=3.4641$).

Our study showed that, most of the patients had Stage IIB after chemotherapy [22 (44.0%)] and it was not statistically significant ($p=0.14706$) ($z=1.4499$).

In our study, higher number of patients had Down stage Result [35 (70.0%)] followed by Same Result [15 (30.0%)] but this was statistically significant ($p=0.00006$) ($z=4$).

Bharadwaj BS et al¹⁸ (2021) examined that breast cancer being a multifactorial disorder outcome depends on various clinicopathological and molecular factors. Four out of 6 pCR cases had preclinical tumor size ≤5 cm.

We showed that, the mean Tumor size of patients was $[7.2880 \pm 1.4822$ (cm)] and mean % of size reduction of patients was $[58.0000 \pm 15.0509]$.

SUMMARY AND CONCLUSION

- In our study, out of 50 patients, most of the patients were 51-60 years of age. Age was statistically significant. The mean Age of patients was $[49.9600 \pm 9.5404]$.
- In our study, all patients had Lymph node involvement and no distant metastasis.
- We found that, most of the patients had tumor in size 5-7 cm followed by Tumor in size 8-10 cm but this was statistically significant.
- We showed that, most of the patients had Stage IIIA. However, Stage IIIB followed by Stage IIIC which was statistically significant.
- It was found that, all patients had Anterior Chemotherapy.
- Our study showed that, Same Lymph node status was higher than down stage Lymph node status but this was not statistically significant.
- We found that, more number of patients had Size reduction 25-50% rest of 50-75%, >75-99% and <25% though it was statistically significant.
- Our study showed that, most of the patients had Stage IIB after chemotherapy and it was not statistically significant.
- In our study, higher number of patients had Down stage Result followed by Same Result but this was statistically significant.
- We showed that, the mean Tumor size of patients was $[7.2880 \pm 1.4822$ (cm)] and mean % of size reduction of patients was $[58.0000 \pm 15.0509]$.

Table 1: Distribution Of Tumor In Size (CM), Anterior Chemotherapy, Lymph Node Status, Stage After Chemotherapy, Stage And Lymph Node Involvement

		Number of patients	%
Tumor in size (CM)	5-7	30	60%
	8-10	20	40%
	Total	50	100%

Anterior Chemotherapy	Yes	50	100.0%
	Total	50	100.0%
Lymph node status	Down stage	23	46.0%
	Same	27	54.0%
	Total	50	100.0%
Stage after chemotherapy	IIA	13	26.0%
	IIB	22	44.0%
	Same	15	30.0%
	Total	50	100.0%
Stage	IIIA	25	50.0%
	IIIB	15	30.0%
	IIIC	10	20.0%
	Total	50	100.0%
Lymph node involvement	Yes	50	100.0%
	Total	50	100.0%

Table 2: Distribution Of Mean Tumor Size(CM) And % Of Size Reduction

	Number	Mean	SD	Minimum	Maximum	Median
Tumor size(CM)	50	7.2880	1.4822	5.0000	10.0000	7.0000
% of size reduction	50	58.0000	15.0509	25.0000	80.0000	60.0000

REFERENCES

1. Mougalian SS, Soulos PR, Killelea BK, Lannin DR, Abu-Khalaf MM, DiGiovanna MP, Sanft TB, Puztai L, Gross CP, Chagpar AB. Use of neoadjuvant chemotherapy for patients with stage I to III breast cancer in the United States. *Cancer*. 2015;121(15):2544–52.
2. Killelea BK, Yang VQ, Mougalian S, Horowitz NR, Puztai L, Chagpar AB, Lannin DR. Neoadjuvant chemotherapy for breast cancer increases the rate of breast conservation: results from the National Cancer Database. *J Am Coll Surg*. 2015;220(6):1063–9.
3. Puig CA, Hoskin TL, Day CN, Habermann EB, Boughey JC. National Trends in the use of neoadjuvant chemotherapy for hormone receptor-negative breast Cancer: a National Cancer Data Base Study. *Ann Surg Oncol*. 2017;24(5):1242–50.
4. M P, M M. Axillary nodal management following neoadjuvant chemotherapy: a review. *JAMA Oncol*. 2017;3(4):549–55.
5. Hunt KK, Yi M, Mittendorf EA, Guerrero C, Babiera GV, Bedrosian I, et al. Sentinel lymph node surgery after neoadjuvant chemotherapy is accurate and reduces the need for axillary dissection in breast cancer patients. *Ann Surg*. 2009;250(4):558–66.
6. Anders CK, Carey LA. Biology, metastatic patterns, and treatment of patients with triple-negative breast cancer. *Clin Breast Cancer*. 2009;9(Suppl 2):S73–81.
7. Wahba HA, El-Hadaad HA. Current approaches in treatment of triple-negative breast cancer. *Cancer Biol Med*. 2015;12(2):106–16.
8. Mamounas EP, Anderson SJ, Dignam JJ, Bear HD, Julian TB, Geyer CE Jr, et al. Predictors of locoregional recurrence after neoadjuvant chemotherapy: results from combined analysis of National Surgical Adjuvant Breast and bowel project B-18 and B-27. *J Clin Oncol*. 2012;30(32):3960–6.
9. McGuire SE, Gonzalez-Angulo AM, Huang EH, Tucker SL, Kau SW, Yu TK, et al. Postmastectomy radiation improves the outcome of patients with locally advanced breast cancer who achieve a pathologic complete response to neoadjuvant chemotherapy. *Int J Radiat Oncol Biol Phys*. 2007;68(4):1004–9.
10. Nagar H, Boothe D, Ginter PS, Sison C, Vahdat L, Shin S, et al. Disease-free survival according to the use of postmastectomy radiation therapy after neoadjuvant chemotherapy. *Clin Breast Cancer*. 2015;15(2):128–34.
11. Choudhary P, Gogia A, Deo S, Mathur S, Sharma D. Neoadjuvant chemotherapy in locally advanced breast cancer: Clinicopathological characteristics and correlation with pathological complete response. 2020.
12. Kunnuru SK, Thiagarajan M, Daniel JM, Singh B. A study on clinical and pathological responses to neoadjuvant chemotherapy in breast carcinoma. *Breast Cancer: Targets and Therapy*. 2020;12:259.
13. Bhattacharyya T, Sharma SC, Yadav BS, Singh R, Singh G. Outcome of neoadjuvant chemotherapy in locally advanced breast cancer: A tertiary care centre experience. *Indian Journal of Medical and Paediatric Oncology: Official Journal of Indian Society of Medical & Paediatric Oncology*. 2014 Jul;35(3):215.
14. El-Mahdy MM, Ibrahim RA, Hamed RM, Elkady MS, Bayoumy WA, Elsayed ZM, Ezz-El-Din MM. Prediction of Response to Neoadjuvant Chemotherapy in Egyptian Patients with Locally Advanced Breast Cancer: The Evolving Role of Tumour Infiltrating Lymphocytes (TILs). *Journal of Cancer Therapy*. 2020 Apr 3;11(4):206–19.
15. Klein J, Tran W, Watkins E, Vesprini D, Wright FC, Look Hong NJ, Ghandi S, Kiss A, Czarnota GJ. Locally advanced breast cancer treated with neoadjuvant chemotherapy and adjuvant radiotherapy: a retrospective cohort analysis. *BMC cancer*. 2019 Dec;19(1):1–1.
16. Tang S, Wang K, Zheng K, Liu J, Zhang H, Tan M, Li H, Li H, Tan X, Liu D, Guo R. Clinical and pathological response to neoadjuvant chemotherapy with different chemotherapy regimens predicts the outcome of locally advanced breast cancer. *Gland Surgery*. 2020 Oct;9(5):1415.
17. Gogia A, Raina V, Deo SV, Shukla NK, Mohanti BK, Sharma DN. Taxane and anthracycline based neoadjuvant chemotherapy for locally advanced breast cancer: institutional experience. *Asian Pacific Journal of Cancer Prevention*. 2014;15(5):1989–92.
18. Bharadwaj BS, Mahanta N, Goswami BC, Bhuyan K. Response to neoadjuvant chemotherapy in locally advanced breast cancers in association with different clinicopathological parameters. *Oncology Journal of India*. 2021 Jan 1;5(1):13.