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# Impact of Neoadjuvant Chemotherapy in Breast Cancer Patients: A Single Center study

Sajid Ali
Medical Oncology, Hayatabad Medical Complex Peshawar

Ayesha Sadia
Mphil Hematology KMU Peshawar

Shehryar Ahmad
Clinical Technologist Health Department Khyber-Pakhtunkhwa

**Abstract:- Due to limited sources in developing countries mostly breast cancer patients usually present in a locally advanced stage with large masses, infected wounds, or ulcers. Nowadays Neoadjuvant chemotherapy is the gold standard for early and locally advanced stage tumor patients as it downstages tumor with the benefit of breast conservation treatment and also kills the micro metastasis to improve survival and also give an insight into the tumor behaviour by assessing its response to chemotherapy. In the current study, 58 patients with localized breast cancer patients enrolled at Hayatabad medical complex Peshawar in the year 2020-21 were assessed for their response to neoadjuvant chemotherapy. Tumor measurements were carried out by baseline TNM staging pathological assessment post-surgery. Complete pathological response was seen in 24.41% (17.24% were stage 2,5.17% were stage 3, partial response was observed in 31.03% (all were stage 3), 17.64% had stable disease(5.17% were stage 2, 20.68% were stage 3), 20% had progressive disease(1.72% were stage 2, 17.24% were stage 3). We found at the end of the study that breast cancers presented in our setup had a higher stage, unpredictable response to chemotherapy; stage 3 was more resistant to chemotherapy.**

***Keywords:-*** *Breast Cancer, chemotherapy, KI67, Progressive disease Tumor.*

## I. INTRODUCTION

1st according to the data by World Health Organization (WHO) an estimated 1.5 million new cases of breast cancer occur per annum throughout the world and is leading cancer in female gender in developing countries and its mortality/incidence relationship is 42.9%, whereas in developed countries it is around 29% [1].In developing countries, the tumor is usually detected at an advanced stage. Factors that may contribute to this in developing countries are age [2], psychological disorders [3], racial and socioeconomic differences, besides the biological behaviour of the tumor.

Breast cancer when diagnosed early has a very good outcome with less aggressive treatment needed and breast conservation surgery can be carried out with good cosmetic outcome without affecting disease management. Nowadays neoadjuvant chemotherapy is the gold standard for locally advanced and even early breast cancer as it downsizes tumors with breast conservation, eradicates micro Mets, and also gives insight into the tumor biology upon surgery post-chemo by assessing the response to chemotherapy. Early breast cancer includes tumors less than 5cm with/without 1-3 ln in the axilla while Locally advanced breast carcinoma, on the other hand, is a relatively heterogeneous stage group, based on its biological, clinical, and pathological behaviour. The locally advanced non-metastatic tumor include: tumors>5 cm, bulky lymph node involvement (N2 or N3), tumor invasion of skin or chest wall, and inflammatory carcinoma [4].It has been known that adjuvant chemotherapy administration improves survival [5]. But administering chemo in the neoadjuvant setting has many advantages. 1st downsizing the tumor, with less extensive surgery needed and improved chances of breast conservation6. 2nd micrometastasis, if present is eradicated with resultant prevention of genetic mutations in metastatic cells, associated with a worse prognosis: as these micro Mets tend to have accelerated growth if primary tumor resected [7] and, also prevent the emergence of drug-resistant subclones in clonal evolution8. Another benefit of neoadjuvant chemotherapy is that it helps to monitor the efficacy of treatment by guiding to identify of chemo response markers.

Many studies which show the effect of chemotherapy on breast cancer do so by comparing patients who had and hadn't chemotherapy. A better approach is to have baseline tumor parameters and then pathological assessment of breast tumor after receiving neoadjuvant chemo. The improved outcome can be expected for Patients with a reduction in tumor volume, surrogate for chemosensitive disease. A valid parameter to assess the effect of chemo on tumors hasn't been established. Also, the response of the tumor to chemotherapy is not a fact till now. Different breast cancer markers have been studied as prognostic factors like HER2, P53, and BCL-2 [9]. Many studies are investigating predictive response factors to chemotherapy. Histopathological tumor response to chemotherapy has also been investigated in a few studies [10].

In the current study tumor characteristics before and after chemotherapy were studied based on pathological response and also pathological TNM staging post-chemotherapy. The main purpose of this study is to assess pathological tumor response to anthracycline and taxane-based chemotherapy.

## II. MATERIALS AND METHODS

### *A. Patients:*

In the current study, 58 patients with localized breast cancer patients enrolled, after written informed consent, at Hayatabad medical complex Peshawar in the year 2020-21 were enrolled. Breast cancer diagnosis and staging were performed via clinical, imaging, and histopatho logical. Patients received 4 cycles of AC( doxorubicin 60mg/m2 and

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cyclophosphamide 600 mg/m2) followed by Taxane 4 cycles (paclitaxel 175mg/m2) and for HER2 positive 4 cycles of trastuzumab ( Herceptin hycleta 600 mg s/c) . the patients then underwent surgery(MRM all) followed by a histopathological response. Enrolment criteria were age 20-70, perfomance≤2, histopathological diagnosis of breast ca, baseline tumor stage via radiological imaging, non-metastatic disease.

*B. Response assessment to Neoadjuvant chemotherapy:*

Union for International Cancer Control (UICC) criteria were used for clinical response assessment. Pathological complete response was the absence of ant tumor deposit in primary and lymph nodes, partial response as > 50% reduction in tumor volume, stable disease between <50% decrease in tumor volume and >25% increase in tumor/clinical mets as progression.

*C. Response Neoadjuvant chemotherapy – pathological tumour testing:*

H& E staining was used for histopathological assessment of tumors. Invasive residual disease was taken into consideration only, and tumor, if found, in primary and/or in axillary lymph nodes was scored according to UICC criteria.

*D. Ethics Approval:*

This study was approved by the ethical committee of Hayatabad medical complex Peshawar. It was conducted in accordance with the Declaration of Helsinki.

## III. RESULTS

Age of patients ranged from 23-67 with mean age of 47 years and standard deviation of 10.31.Majorityof patient were in stage of postmenopausal status whereas Lump in the breast was the chief presentation. The tumour size on physical assessment was almost 7 +/- 3.3 cm (2-15 cm).

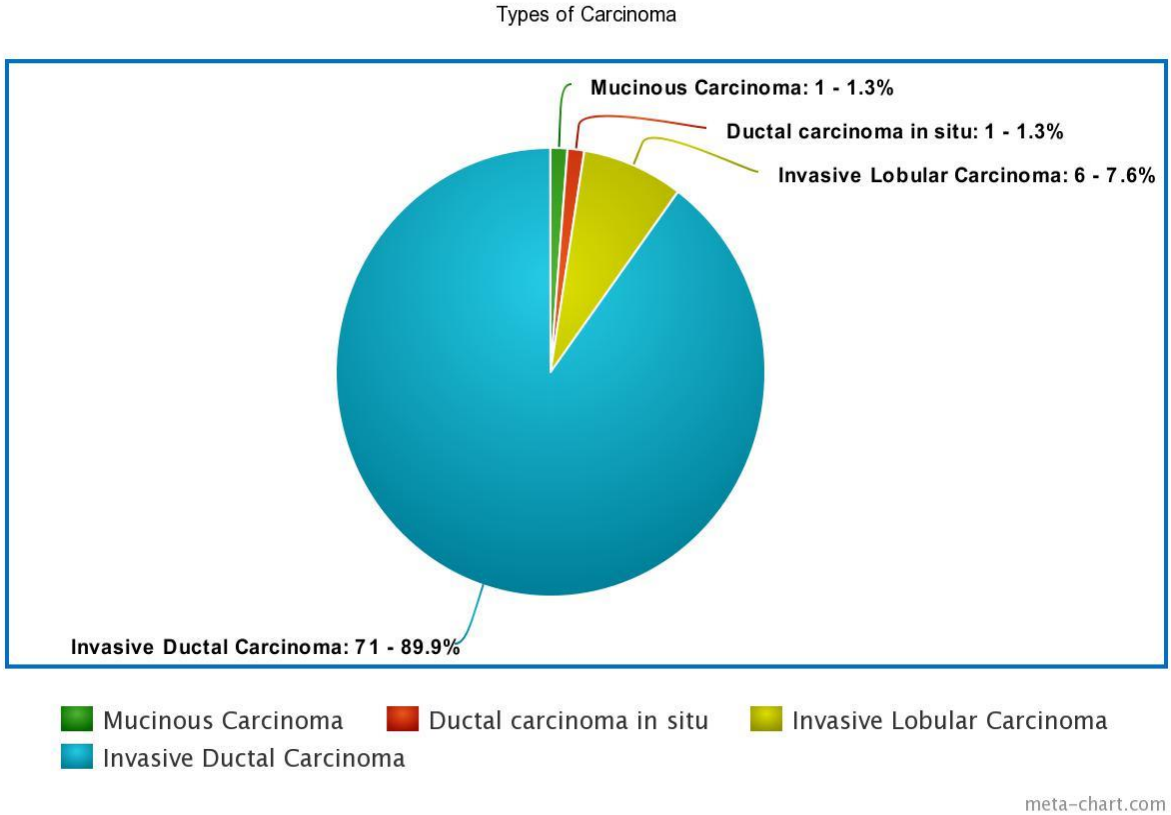


Fig. 1: Types of Carcinoma

As per type of carcinoma about 89.9% suffering from invasive ductal carcinomas (n=71) followed by invasive lobular carcinoma 7.6% (n=6), whereas 1.3% each had mucinous carcinoma and DCIS.(n=1) as shown in figure 1.

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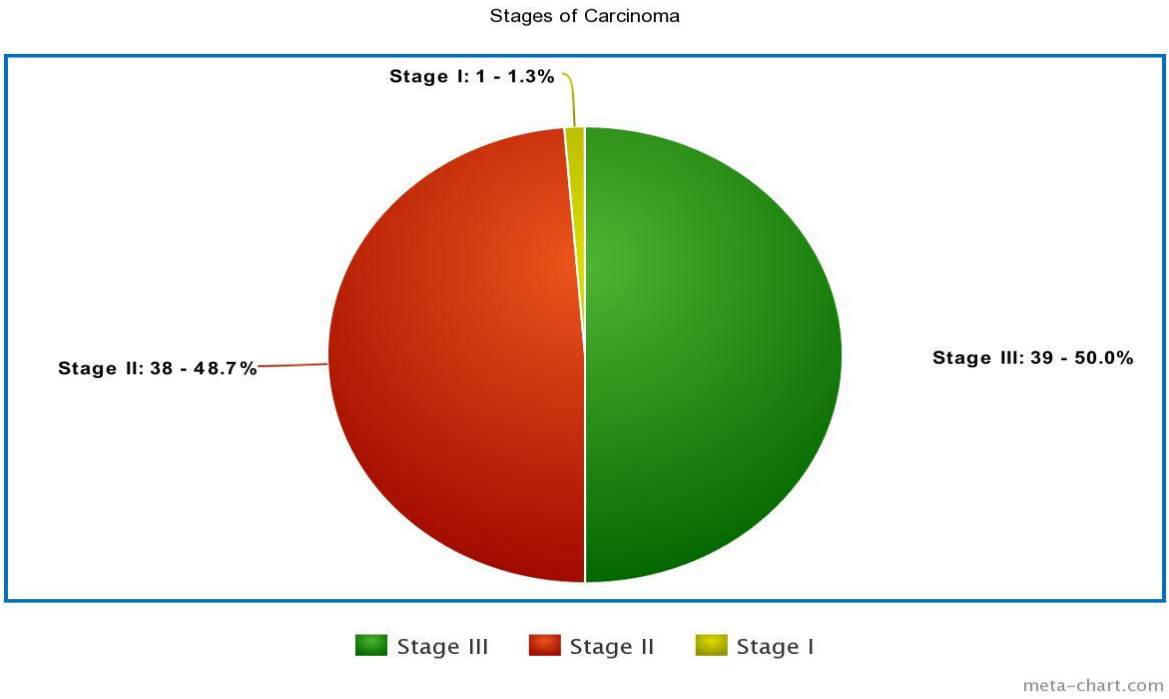


Fig. 2: Stages of Carcinoma

Data regarding stages of carcinoma reveals Stage III comprise of 39 (50%) patient followed by stage II having 38(48.8) patient whereas stage I (1.2%) have only 01 patient respectively as shown in figure 2.

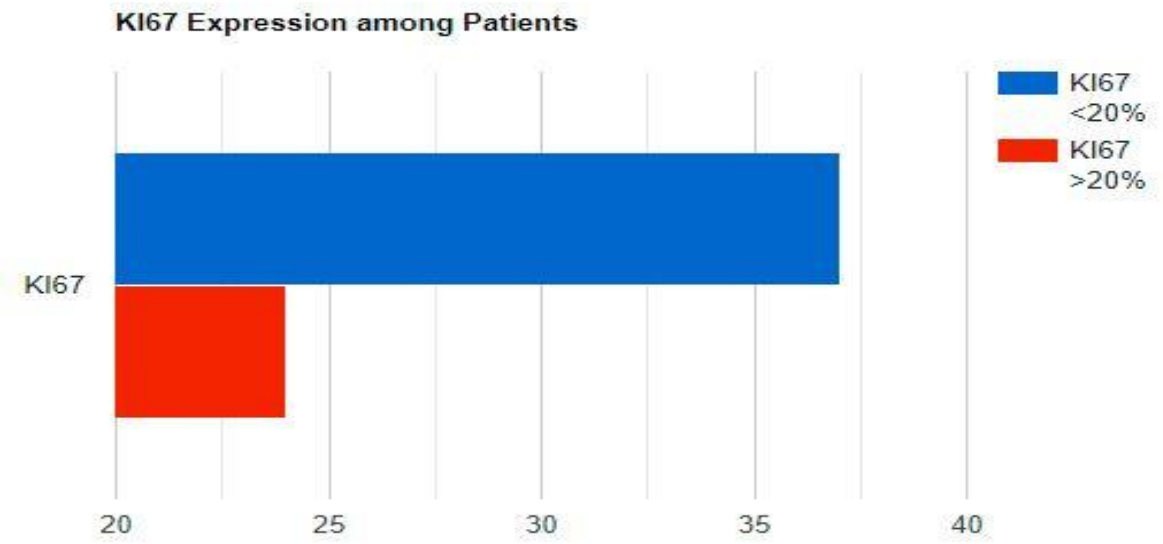


Fig. 3: KI67 Expression among patients

Among the study participant 36 patients have KI67 expression is less than 20% whereas 24 patients have KI67 expression greater than 20% respectively as shown in figure 3. Cross tabulation of KI67 expression with stage of cancer reveals 28 patients with KI67 expression is less than 20 percent whereas 4 patient with stage 2 have KI67 expression of greater than 20.

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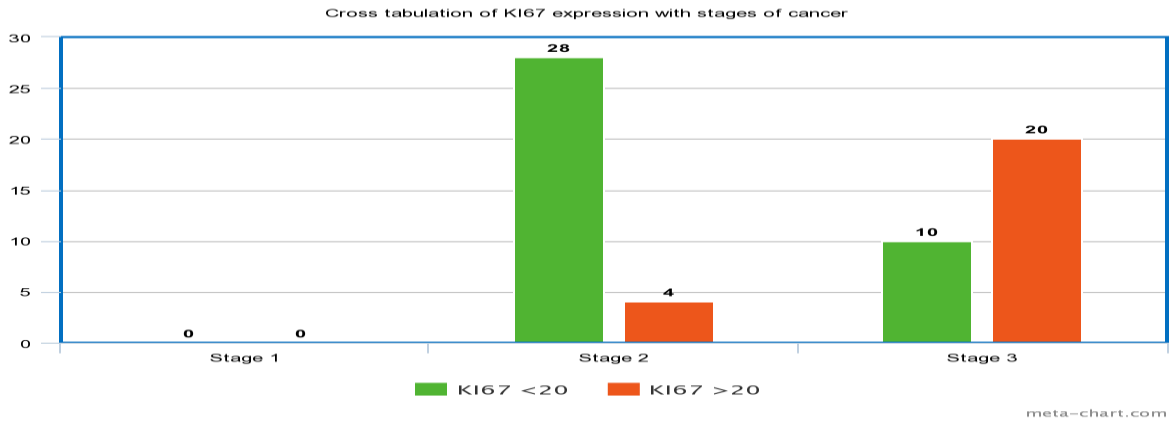


Fig. 4: KI67 Expression with different stage of disease

Similarly in stage 3 overall 10 patients have KI67 expression is less than 20 percent while 20 patients have KI67 expression of greater than 20 percent respectively. None of the patient of stage 1 in both KI67 expression of less and greater than 20 is found as shown in figure 3.

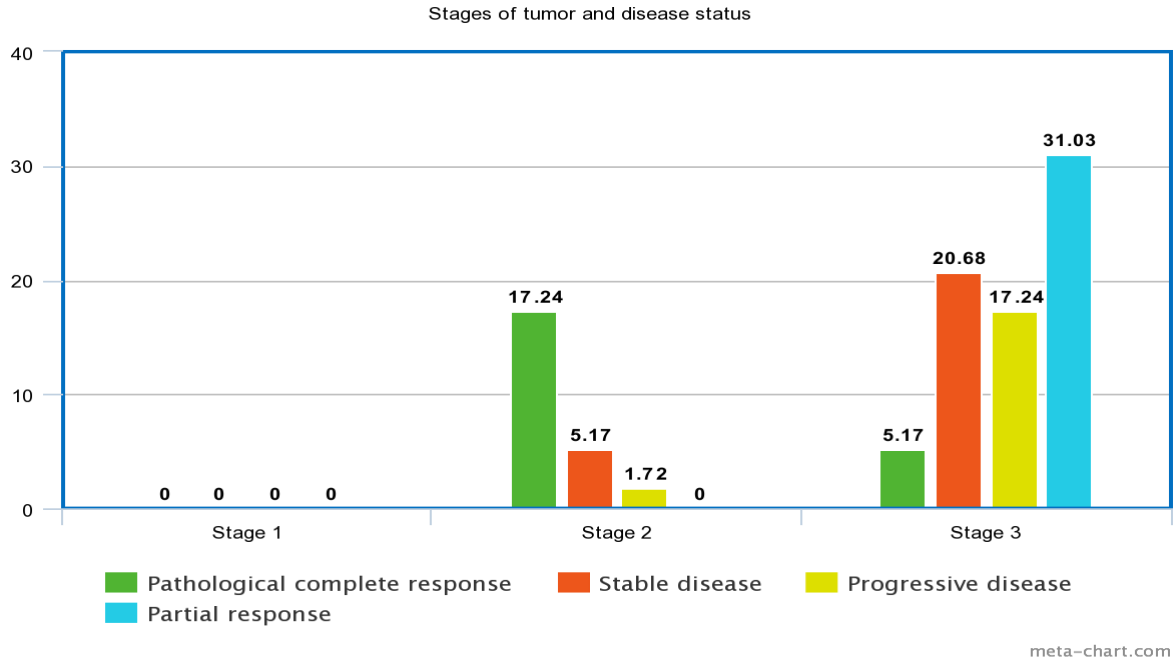


Fig. 5: Stage of Tumor and disease status

All of the patients underwent modified radical mastectomy, Over all response rate ORR was 71.05%, whereas pathological complete response was observed in 22.41% among which 17.24% were stage 2 and 5.17% were stage 3 respectively. 31.03% patients had partial response(all patient were in stage 3), while 17.64% patients had stable disease(among which 5.17% were stage 2, while 20.68% were in stage 3). 20% patients had a progressive disease (1.72% among which are in stage 2 while 17.24% were in stage 3) as shown in figure 5.Of these progressive disease patients 5 had developed bone Mets who then received bisphosphonates.

## IV. DISCUSSION

Neoadjuvant chemotherapy has a significant role in breast cancer now and is now being considered as the gold standard for any breast cancer patient with a tumor beyond T1. Also, neoadjuvant chemotherapy can be used when T> 5 cm, positive axillary lymph nodes, Her2 positive, TNBC, Small breasts compared to tumors who wish to conserve their breast. Post chemotherapy positive axillary lymph node is a poor predictor of metastasis [11-12].

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In the current study, we found ORR 71.05% with 22.41% patients had pCR. pCR post neoadjuvant chemotherapy is considered a surrogate marker for long-term outcomes[13-15]. But response varies with different demographics of patients, different histological subtypes, and also the type of neoadjuvant chemotherapy used due to the heterogeneous nature of breast tumors based on the clinical, molecular, biological and genetic grounds14. Response varies in breast cancer with clinical complete response 7-65% and pathological CR 4-29%, especially in locally advanced breast cancer [16]. Low pCR observed for locally advanced breast cancer may be due to large tumor sizes and also tumors may be chemo resistant [17].

In the present study, the overall clinical response rate was 71.05.6% (SD plus PR and pCR). Patients achieving clinical complete response can still have a viable tumor on histopathological specimen examination. Comparing the current study with Garbhi [18] had a clinical complete response of 14%, PR 49%, and in another alvarado et al [19]had a clinical complete response in 12% and pR of 28% of patients respectively.

In our study, the pCR in TNBC was 42.85%, HR 28.57%, Her2 21.42%, and 7.14% in the triple positive. A study by dr petal [20] showed similarly good pCR in ER-positive tumours, while migleta [21]study showed good pCR in her2 positive tumorsKim et al [22] found higherRR inTNBC like our study.pCR was higher in patients with age > 45 and in menopausal women 57.14% and was low in premenopausal women and age <45 42.85%.its in contrast with de prete [20] which said good path cr in premenopausal women wile resend say no relationship of menopausal status with pCR. pCR was higher in grade 2 histology 57.14% while 42.85% in grade 3 tumors. On the other hand, Awad study23 and resend24 found higher responses in higher-grade tumors. All of the patients who went into CR had IDC, none of the 6 ILC went to pCR while one metaplastic Histology become metastatic while on treatment, implying that tumor histology has a role in tumor response.

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## V. CONCLUSION

The neoadjuvant chemo combo of anthrycline and taxane based downstage tumour as well as in axilla with better response and higher pCR. pCR higher in TNBC andluminal A type breast ca respectively.

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