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Response Of Neoadjuvant Chemotherapy Based On Different Subtypes Of Breast Cancer

Dr Advait.M.K[1], Dr D. Bhargavi[2], Dr Ravi Teja.C[3], Dr P.Sindhu[4], Dr B.Manilal[5],Dr.V.Aditya[6]

1,3,6} Senior Resident Department of Medical Oncology SVIMS
2}Associate Professor and Head of Department (HoD) Department of Medical Oncology Sri Venkateswara Institute of Medical Sciences (SVIMS)
4}Assistant Professor Department of Medical Oncology SVIMS
5}Associate Professor Department of Surgical Oncology SVIMS

Abstract-
Breast cancer is the most common malignancy in the world and the second leading cause of mortality. Patient s diagnosed with breast cancer are staged as per AJCC 8th edition and are classified based on different subtypes based on the hormonal, Her2 neu and Ki67 receptor status, they are classified as Luminal A, B, Her 2 neu enriched and TNBC, The response of patients to neoadjuvant chemotherapy varies depending upon the subtype. Here we discuss about the response of patients based on response to neo adjuvant chemotherapy vase dob the subtype. The current study undertaken in the department of medical oncology of our department to see the response of Neoadjuvant chemotherapy to various subtypes of carcinoma breast.

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I. Introduction

According to GLOBOCAN 2020 carcinoma breast is the most common cancer in India with an incidence of 1.78 per lakh of population and it accounts for 90,498 deaths [1]. Breast cancer is a heterogeneous disease and mainly classified into four molecular subtypes Luminal-A, Luminal-B, HER-2-neu and triple negative and is staged now as per AJCC 8th edition, The number of patients presenting in various stages depends on the screening protocol in various countries, patient knowledge about cancer, referring physician etc. Neoadjuvant chemotherapy is defined as the administration of systemic therapy prior to surgical removal of a tumour, The initial rationale of using neoadjuvant chemotherapy was to convert patients with locally advanced disease which were inoperable tumours into operable tumours {2-5}. In case of breast cancer neoadjuvant chemotherapy is used for locally advanced breast cancer, inflammatory breast cancer, and downstaging of large tumours to allow for breast conservation therapy it is also now extended to clinically node negative breast cancer patients with unfavourable tumour profiles, in whom adjuvant systemic therapy is predicted. {6,7}. Definition of complete pathologic response as a surrogate endpoint predictor of long-term clinical benefit has remained variable. The three most used definitions are absence of invasive cancer and in situ cancer in the breast, and axillary lymph nodes (ypTo ypNo), irrespective of ductal carcinoma in situ (ypTo/is ypNo), and absence of invasive cancer in the breast irrespective of ductal carcinoma in situ or lymph node involvement (ypTo/is). Partial response is defined as the presence of residual disease in the primary lesion or node after neoadjuvant chemotherapy.

II. Materials and methods

This is a prospective study done on carcinoma breast patients attending the breast clinic of our hospital from {JULY 2021 to JUNE 2022}. All patients who were histologically confirmed were enrolled in the study, . As a part of staging of the cancer contrast enhanced CT scan of the chest and abdomen along with bone scan or a whole-body PET CT scan was done. Patient subtyping of the cancer was done with IHC for ER, PR, and HER 2 neu, If Her 2 neu was equivocal FISH was done to confirm positivity.

III. Results

A total of 183 patients were treated in our hospital during this period.
The median age of the study population was 51.8 years, majority of the study population belongs to the 41-50 years which constituted 38.7%
Most patients belonged to Stage III and it constituted 46.4% of the study population

Majority of the patients in the study population belonged to luminal subtype 56%(n=102) with 35%(n=63) belonging to luminal B and 21%(n=39) belonging to luminal A subtype with almost equal distribution in TNBC and HER 2 neu enriched subtype.

Majority of the patients received adjuvant chemotherapy 53% (n=98) followed by 37 %(n=67) receiving neoadjuvant chemotherapy 37 %(n=67) and 10 %(n=18) receiving palliative chemotherapy Of the 37 %(n=67) patients who received neoadjuvant chemotherapy complete response was achieved by 49 %(n=33) irrespective of the type of chemotherapy regimen used.

Response	Number	Percentage (%)
Partial	34	51
Complete	33	49
	67	100

Response to neoadjuvant chemotherapy based on molecular subtype

	Number	Partial response	Complete response
Luminal A	15	9	6
Luminal B	20	7	13
Her 2 neu enriched	16	10	6
TNBC	16	9	7

From our study it can be seen that the percentage of population with maximum complete response was in Luminal B followed by TNBC and then Luminal A and followed by Her 2 neu subtype.

IV. Discussion.

The management of breast cancer has evolved throughout the years with initial management being with chemotherapy and the current management is based on the breast cancer subtype, which is determined by the expression of ER, PR, and HER2 neu. Response to neoadjuvant chemotherapy {NAC} is evaluated by the change in tumour size from pretreatment clinical and/or radiologic measurement to post-treatment status. The spectrum of response to neoadjuvant chemotherapy varies from complete response, partial response, to non-response. This concept is the same in breast tumours as well as axillary lymph nodes. Studies have shown that the rate of response to therapy varies from 15% to 30% depending on the type of tumour and the type of chemotherapy used .Patients who achieve complete response to neoadjuvant chemotherapy experience better outcomes, that is, long-term disease-free survival, and better overall survival when compared to those patients whose tumours do not respond to therapy{8}.Small tumour size, high tumour grade, high proliferation rate, tumour necrosis, and presence of tumour-associated lymphocytes are considered predictors of better response to neoadjuvant chemotherapy. It has been found that higher pCR was seen in TNBC and HER2-positive subtypes. In estrogen receptor (ER)-positive breast cancer (BC), young age is associated with poor prognosis. While very young patients respond better to chemotherapy, chemotherapy is less effective in ER-positive tumours than in ER-negative tumours pCR after NAC is associated with an improved DFS. It was observed that not all TNBC achieve pCR and some Luminal subtypes patients respond to NAC. Ki 67 and tumour infiltrating lymphocytes {TILs} are some potential biomarkers which can predict therapeutic response to NAC but is underutilised in clinical practice{9} Tumour-infiltrating lymphocytes are a mixture of proinflammatory immune cells such as cytotoxic CD8+ T-cells, natural killer, dendritic, and T-helper cells, and those with immune suppressor action including B-cells and regulatory CD4+ T-cells that are found in both the tumour and the surrounding microenvironment of breast cancer.{10,11}. Currently, the change in the rate of Ki-67 as a proliferation marker is regarded as a marker for response to neoadjuvant chemotherapy, particularly in patients with hormone receptor positive tumours who receive endocrine therapy {12-14}. The reason for the varied response to chemotherapy in our study may be due to small sample size and the patients were not able to maintain the chemo intensity as the study was conducted during the covid time. Molecular signatures are currently being used to identify low risk patients who are less likely to benefit from chemotherapy regardless of nodal status or in the setting of HR+ node-negative disease. Such patients have been shown to have low rates of response to chemotherapy and very low rates of early recurrence. Confirmation of chemotherapy benefit in molecularly low risk patients will be forthcoming from the TAILORx and MINDACT trials {15}. In a pooled analysis of German neoadjuvant breast cancer trials, it was found that higher numbers of cycles and higher cumulative doses of both, anthracyclines and taxanes, and use of capecitabine and trastuzumab were associated with a clinically relevant increase in pCR. When stratifying according to hormone receptor and HER2 status, they found that the number of cycles to be particularly relevant in patients with HR-positive tumours, and cumulative anthracycline dose in patients with HER2-negative tumours {16}.

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