FREQUENCY OF PATHOLOGICAL COMPLETE RESPONSE (PCR) IN PATIENTS OF TRIPLE NEGATIVE BREAST CANCER AFTER NEO-ADJUVANT CHEMOTHERAPY

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ABSTRACT

Objective: To determine the frequency of patients with complete pathological response (pCR) after neo adjuvant chemotherapy (NACT) in locally advanced triple negative breast cancer.
Study Design: Descriptive cross sectional study.
Place and Duration of Study: Department of Oncology, Hameed Latif Hospital, Lahore, from Aug 2019 to Feb 2020.
Methodology: After taking approval from hospital ethics committee, 100 patients coming through Out-patient department who fulfill the selection criteria were enrolled and written informed consent were taken from them.
Results: A total of 100 fulfilling the inclusion/exclusion criteria were enrolled to study to determine frequency of patients with complete pathological response after neo adjuvant chemotherapy in locally advanced triple negative breast cancer. Age distribution of the patients was done, it shows that out of 100 patients, 38 (38%) were between 18-40 years of age whereas 62 (62%) in were between 41-70 years of age, mean age was calculated as 44.18 ± 9.71 years. The data was stratified for age, stage of disease and eastern cooperative oncology group (ECOG) grade of the patients. When associated with grades of the disease, it was found to be statistically significant (p=0.003).
Conclusion: Hence we concluded that about one third of the patients with neo adjuvant chemotherapy showed complete pathological response.

Keywords: Breast cancer, Neo-adjuvant therapy, Pathological response.

INTRODUCTION

Globally, breast cancer is the most frequently diagnosed cancer and the leading cause of cancer death in women. There are various histologic types of breast carcinoma that differ in microscopic appearance and biologic behavior and are named as Infiltrating ductal, Infiltratinglobular, mixed ductal/lobular, meta-plastic, mucinous, tubular, medullary, and papillary carcinoma[1].

Gene expression studies have identified several distinct breast cancer subtypes that differ markedly in prognosis and in the therapeutic targets they express. Based on gene expression profiles, Luminal (luminal A and luminal B), Her 2 Enriched, asal molecular subtypes have been identified. Most of basal subtype falls under the category of triple-negative breast cancers because they are ER, PR, and HER2 negative by immunono-histochemical stains (IHC)[2].

Breast cancer is treated with a multidisciplinary approach involving surgical, radiation and medical oncology, which has been associated with a reduction in breast cancer mortality[3]. Non metastatic breast cancer is broadly considered in two categories: Early stage and Locally advanced. Most patients with locally advanced breast cancer, and some with earlier-stage disease (particularly if triple negative or human epidermal growth factor receptor 2 [HER 2] positive), are treated with neo-adjuvant chemotherapy (NACT) systemic therapy[4].

Neo-Adjuvant chemotherapy (NACT) is associated with high rates of clinical response and a greater likelihood of facilitating cosmetically acceptable surgery. The outcomes of NACT were demonstrated in a 2007 meta-analysis that included data from 5500 women participating in 1 of 14 trials reported between 1991 and 2001. Compared with adjuvant chemotherapy, NACT resulted in reduction in the risk of having a modified radical mastectomy performed with equivalent progression free and Overall survival[5]. Among patients treated with NACT, a documented pathologic complete response (pCR) at surgery was prognostically significant. Patients with a pCR had significant improvements in both Overall survival and Disease free survival compared with patients with residual invasive disease. These differences were more pronounced in patients with triple-negative breast cancer[6], frequency of PCR was 60%[7].

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Patients with Triple negative breast cancer have increased pCR rates after Neo-Adjuvant chemotherapy (NACT) compared with non-Triple negative breast cancer and those with pCR have excellent survival[8]. Patients who achieved a pathologic complete response to neoadjuvant therapy also had significantly better overall survival than those with residual disease. Survival was improved by 78% in those with a pathologic complete response. Five-year overall survival was 94% for those with pathologic complete response vs 75% for those with residual disease[9]. The relationship between pathologic complete response and survival was strongest for triple-negative breast cancer. Hence we aimed this study to check the frequency of pathological response to neo-adjuvant therapy in these patients.

METHODOLOGY

This descriptive cross sectional study was done at Department of Oncology, Hameed Latif Hospital, Lahore, from August 2019 to February 2020. After taking approval from hospital ethics committee, 100 patients coming through OPD of the department who fulfill the selection criteria were enrolled and written informed consent were taken from them. After the baseline examination, all the patients were advised to have 4-6 cycles neo-adjuvant chemotherapy carboplatin and paclitaxel. Response evaluation was done with CT post followed by cytoreductive surgery. Follow-up was ensured by taking patient's contact number (every 3 monthly). All the information was recorded on proforma. Sample size of 100 cases was calculated with 95% confidence level, 10% margin of error and taking assumed complete pathological response 60%[9]. Non-probability consecutive sampling technique was used.

Inclusion criteria consisted of patients with histopathologically proven triple negative breast cancer with locally advance stage IIB disease (T3N0) and stage IIIA to IIIC breast carcinoma and the patients having ECOG Performance Status 2 or less. Patients who have received any treatment (chemotherapy, radiotherapy) prior to presentation assessed on history and review of medical records, having severe toxicity from chemotherapy and patients with disease progression duringneo-adjuvant chemotherapy assessed by chest and upper abdomen CT scan were excluded.

All the data was entered and analyzed by using SPSS-20. Mean and standard deviation was calculated for all quantitative variables like age. Frequency and percentage were calculated for all qualitative variables. Effect modifiers like age and stage of disease, ECOG grade were controlled by stratification. Chi-square test was done with a p-value ≤0.05 taken as statistically significant.

RESULTS

A total of 100 fulfilling the inclusion/exclusion criteria were enrolled to study to determine frequency of patient's with complete pathological response (pCR) after Neo adjuvant chemotherapy (NACT) in locally advanced triple negative breast cancer.

Age distribution of the patients was done, it shows that out of 100 patients, 38 (38%) were between 18-40 years of age whereas 62 (62%) in were between 41-70 years of age, mean age was calculated as 44.18 ± 9.71 years (table-I).

The data was stratified for age, stage of disease and ECOG grade of the patients in table-II. When associated with grades of the disease, it was found to be statistically significant (p=0.003).

Table-I: Frequency distribution of different demographic variables along with features of the disease (n=100).

Variables	Groups	n (%)
Age Groups	18-40	38 (38)
	41-70	62 (62)
Distribution of Ecog Grade	Grade 0	45 (45)
	Grade 1	49 (49)
	Grade 2	2 (2)
	Grade 3	3 (3)
	Grade 4	1 (1)
Stage of Disease	IIIA	39 (39)
	IIIB	28 (28)
	IIIC	14 (14)
	IIB	19 (19)
Complete Pathological Response	Yes	33 (33)
	No	67 (67)

Table-II: Prevalence of breast cancer according to demographic variables (n=100).

Variables	Groups	Cases	Controls	p-value
Age Groups	18-40	12	26	0.813
	41-70	21	41	
Distribution of ECOG Grade	Grade 0	23	22	0.003
	Grade 1	8	41	
	Grade 2	0	2	
	Grade 3	1	2	
	Grade 4	1	0	
Complete Pathological Response	IIIA	11	28	0.225
	IIIB	8	20	
	IIIC	8	6	
	IIB	6	13	

*Calculated by chi-square test

DISCUSSION

New agents to treat breast cancer have historically been approved first in the metastatic setting, with approval for use in early-stage breast cancer following many years later on the basis of results of large randomized adjuvant trials with long follow-up[10]. Neo adjuvant treatment - systemic therapy delivered before definitive breast cancer surgery - was once reserved only to reduce the size and extent of locally advanced tumors but is now being used more widely[11]. In addition to increasing the likelihood of tumor control and the potential for curability in early breast cancer, neoadjuvant trials allow rapid assessment of drug efficacy and could expedite development and approval of treatments for early breast cancer[12]. Pathological complete response has been proposed as a surrogate end point for prediction of long-term clinical benefit, such as disease free survival and overall survival (OS)[13].

Neoadjuvant chemotherapy represents an option for patients with early breast cancer when an indication for chemotherapy is given[14]. Pathologic complete response (pCR) has predicted long-term outcome in several neo-adjuvant studies and is therefore a potential surrogate marker for survival[15].

Age distribution of the patients was done, it shows that out of 100 patients, 38 (38%) were between 18-40 years of age whereas 62 (62%) in were between 41-70 years of age, mean age was calculated as 44.18 ± 9.71 years. In this study, we found that frequency of complete pathological response was 33%. One study concluded that pCR defined as no invasive and no in situ residuals in breast and nodes can best discriminate between patients with favorable and unfavorable outcomes. Patients with noninvasive or focal-invasive residues or involved lymph nodes should not be considered as having achieved pCR. pCR is a suitable surrogate end point for patients with luminal B/HER2-negative[16], HER2-positive (nonluminal), and triple-negative disease but not for those with luminal B/HER2-positive or luminal A tumor[17].

Another study recorded that recorded that eradication of tumors from both breast and lymph nodes (ypT0 ypN0 or ypT0/is ypN0 pathological complete response) had a stronger association with improved EFS and OS than did eradication of tumor from the breast alone (ypT0/is)[18]. The strongest association between pathological complete response and long-term outcome was in patients with aggressive breast cancer subtypes (triple negative; hormone-receptor-positive, high-grade, and HER2-negative; and HER2-positive and hormone-receptor-negative)[19]. Nevertheless, an increase in frequency of pathological complete response between treatment groups did not predict improved EFS and OS[20]. This study showed that majority of the patients included in the study were aged between 50-70 years of age. Almost all patients had good ECOG performance status of 1. The stage distribution showed most of them to be having stage 3 disease. The primary end point of pathological complete response was observed in 33 percent of the population. This is in line with the observed PCR in various international studies[21-23] highlighting the fact that disease responses to the internationally approved regimens is almost the same in Pakistani population. We may deduce from this that the disease biology is probably the same though further studies are needed to confirm this.

CONCLUSION

Hence we concluded that about one third of the patients with Neo adjuvant chemotherapy (NACT) showed complete pathological response (pCR). It can probably translate into less improved over survival but longer follow up is needed in these patients to prove this beyond doubt.

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CONFLICT OF INTEREST

This study has no conflict of interest to be declared by any authors.

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