

RESEARCH ARTICLE

Assessment of Clinico Pathological Factors as Predictive Markers in Response to Neoadjuvant Chemotherapy in Locally Advanced Breast Cancer (LABC)

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Abstract

Background: A good plan of management is extremely important for the personalized management of breast cancer. In locally advanced breast cancer, neoadjuvant chemotherapy has a vital role in good subsequent management. There are some predictors for the assessment of clinical and pathological response.

Aim of the Study: To observe the clinical and pathological factors as predictors for responsiveness of NACT in LABC patients.

Methods: It was a cross-sectional comparative study that was conducted among the patients of the Department of Surgical Oncology of NICRH from October 2016 to September 2017. Initially, all the patients were enrolled by purposive sampling. After that, they were scrutinized by eligibility criteria. One hundred patients were selected. A pre-formed, structured, peer-reviewed data collection sheet was prepared, which was used to collect data. Data were compiled, edited, managed and analyzed. The results were tabulated in table and figure form. Data analysis was done by chi-square test. The p-value was significant at <0.05.

Result: Out of the total, 42% and 28% belonged to the 41-50 years and 31-40 years age group respectively. The mean age was 44.51 ± 10.77 years, and the age range was 22-73 years. Among 100 patients, 76% had a BMI between 18.5 and 24.99. Subsequently, 13% of patients had it between 25 and 29.99. The mean BMI of the respondents was 23.81 ± 2.36 . The BMI range was 17.83-31.13. 86% of patients were homemakers, 95% were married, and 92% had a history of breastfeeding. Out of 100 patients, 6% had a positive family history of breast cancer. Among 100 patients, 69% never took any form of hormonal contraceptive in their lifetime. Out of 100 patients, 87% patients were pre-menopausal, whereas the rest 13% were postmenopausal. Out of 100 patients, 80% presented with a lump, and the rest, 20% presented with lump and ulceration, and 54% had this lump on the left side. 75% of patients manifested regional disease, whereas 25% of patients manifested local

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disease out of 100 cases, 62% of patients suffered <4 months duration, and subsequently, 35% of patients experienced symptoms from 4-6 months. Only 3% noticed clinical features for more than 6 months. Out of 100 patients with LABC, there was no such a patient with a lump size <2cm, but 13% of patients responded well after NACT as they were found in this group. Initially, 5% of patients belonged to lump size 2-5cm, which was increased to 67% after NACT. On the other hand, 95% of patients had lumps>5cm in maximum diameter, which was reduced to 20% after NACT. The p-value was found to be significant. 76% of patients had pre-NACT palpable axillary lymph nodes, which dropped down to 65% after NACT intervention; on the contrary, 27% fixed axillary lymph nodes were reduced into 15% fixed axillary lymph nodes. Before NACT, 8% of patients had palpable ipsilateral supraclavicular lymph nodes, which reduced and became 4% after the implementation of NACT. Out of 100 LABC patients, 70% received an AC regimen, and 30% received an FEC regimen. Among 100 LABC patients, clinical response was observed at 77% as PR and 13% as CR. 8% and 2% of patients manifested PD and SD as clinical response (p=0.01 and 0.039 respectively), whereas age, clinical tumor size, lymphatic and vascular invasion, and molecular subtypes were the significant predictors for pathological response.

Conclusion: Most of our patients showed partial response. However, from the point of view of predictive markers of NACT, clinically palpable lymph nodes, as well as chemotherapy, are the influencing factors for good clinical response. In contrast, age, clinical tumor size, lymphatic and vascular invasion and molecular subtypes are excellent markers for pathological response.

Keywords: Assessment, Clinic Pathological, Predictive Markers, Neoadjuvant Chemotherapy, Locally Advanced Breast Cancer (LABC).

1. Introduction

Breast cancer is the most frequent malignancy among Bangladeshi women. In the year 2014, the total female deaths due to cancer in Bangladesh was 41,900. Among these deaths, breast cancer-related death was 16.9%. It was the second leading cause of death in the total population and the leading cause among women [1]. Locally advanced breast cancer (LABC) continues to be a major and difficult disease to treat, especially in unscreened populations. It represents a heterogeneous group of tumours ranging from slowly growing neoplasm to rapidly proliferating and aggressive ones but without evidence of distant metastasis (M0). The management of LABC has revolutionized over the last 3 decades and includes a multidisciplinary approach with neoadjuvant chemotherapy (NACT), surgery, adjuvant systemic therapy, and radiotherapy. Multiple clinical trials have shown that patients who achieve a complete pathological response (PCR) after NACT have improved survival [2]. Responses to neoadjuvant (before surgery) chemotherapy are categorized into clinical and pathological responses. Evaluating chemotherapy response is essential to predict survival rate and to guide future chemotherapy. Clinical responses can be evaluated by two criteria, i.e. the WHO and Response Evaluation Criteria in Solid Tumor (RECIST). Both criteria provide an evaluation based on an assessment of reduced tumour size [3]. Several investigations have reported the importance of clinical/pathologic complete response to neoadjuvant chemotherapy as a factor in improved treatment outcomes, resulting in survival rates up to 70% [4]. However, this prognostic factor is assessed at the time of surgery, when the window for optimizing a neoadjuvant treatment is closed. Standard clinical measures based on anatomic information from the physical assessment, mammography and conventional B-model ultrasound are often unable to objectively evaluate treatment response early during the treatment period since functional changes related to microscopically evident tumour death may precede macroscopic anatomic changes. Recent studies have highlighted the importance of early detection of a patient's refractory to neoadjuvant chemotherapy, as it has been demonstrated that early salvage treatment for chemotherapy-resistant tumors with radiation and surgery can result in a survival rate of 46% at 5 years [5]. Therefore, imaging for early probing of the extent of therapy response is crucial [6]. Most of the breast cancer patients receive chemotherapy at some phase of their illness, but only about half of them benefit from it. Since the inception of cytotoxic treatment for cancer, the question of why some patients respond to therapy while others do not has been asked. So, it can be known before the predictors of responsiveness that all patients need not undergo exposure to these cytotoxic agents. Besides, elucidation of the basic

mechanism behind the response to cytotoxic agents can be possible by identifying and understanding the predicted response. An exact focus on the identification of "predictive markers" that are associated with chemotherapy sensitivity, especially those producing PCR, can reduce unnecessary overtreatment. NACT in LABC provides the best opportunity to assess tumour response in vivo and, thus, tailor the treatment. So, it is assumed that all chemotherapy cannot be chosen particularly for a particular patient. Some predictive factors can guide clinicians to determine which chemotherapeutic agent is perfect for which patients. Or it may be stated that the ongoing chemotherapy in a patient will work perfectly or not. Various studies have analyzed a series of tumour-related characteristics (such as age, menstrual status, tumour size, node status, grade and type of tumour) and certain biomarkers (such as EgR, PgR, Her2, Ki-67, p53, BCl2, BAX, p21, Topo IIx, NF-kB, apoptotic index, tumour cellularity, mitosis) for predicting response to NACT with inconsistent results [7]. Although the effectiveness of therapy can be assessed according to clinical, radiological, or pathological response, the period of Disease-Free Survival (DFS) or Overall Survival (OS), the Pathological Complete Response (PCR) is the most predictive parameter for survival [8]. The PCR is considered when there is complete eradication of the locoregional disease. The main aim of this study is to identify the clinic pathological predictive markers associated with NACT in LABC patients.

2. Methodology and Materials

It was a cross-sectional comparative study which was conducted among the patients of the Department of Surgical Oncology of NICRH from October 2016 to September 2017. Initially, all the patients were enrolled by purposive sampling. After that, they were scrutinized by eligibility criteria. One hundred patients were selected. A pre-formed, structured, peer-reviewed data collection sheet was prepared, which was used to collect data. Data were compiled, edited, managed and analyzed.

- Inclusion criteria
- Patients with LABC (AJCC stage III) (Wittekind et al., 2004) include T0, T1 or T2 with N2 disease.
- T3 tumor with N1 or N2 disease.
- T4 tumor with any N.
- Any T with N3 regional lymph node involvement.

- Exclusion criteria
- History of prior breast surgery for malignancy.
- Chemotherapy.
- Radiotherapy.
- Hormone therapy.
- Patients with metastatic disease (M1) at presentation.

2.1 Ethical Consideration

There is a minimum physical, psychological, social and legal risk while taking history, physical examination and investigations. Proper safety measures were taken at every step of the study. Only the researcher was allowed to access the collected data. Ethical clearance was obtained from the Institutional Review Board (IRB) of NICRH to undertake the current study. According to the Helsinki Declaration for Medical Research involving Human Subjects 1964, all the patients were informed about the study design, the underlying hypothesis and the right of the participants to withdraw themselves from the research at any time, for any reason. Informed written consent was obtained from each subject who voluntarily provided consent to participate in this study.

2.2 Study Procedure

All patients were confirmed to have invasive breast cancer by analysis of 14G to 16G core needle biopsy. The sample was assessed for predictive pathological markers of response to NACT, including histopathology, grade, ER, PR, Her2, Ki-67, and p53, before starting NACT. Clinical markers were evaluated beforehand by history, clinical examination and imaging prior to being subjected to chemotherapy. All patients were treated by standard AC [cyclophosphamide (600mg/m2), Adriamycin (60mg/m2)] or FEC [Flurourucil (500mg/m2), epirubicin (100mg/m2) Cyclophosphamide (500mg/ m2)] combination of NACT for 4 cycles. After NACT, the clinical response of the primary breast cancer was assessed and graded.

2.3 Statistical Analysis

Statistical analysis of the data was performed using SPSS, version 16 (SPSS, Inc., Chicago, IL, USA). The relationship between the tumour reduction rate per chemotherapy cycle and the different predictive markers of response (age, tumour size, node status, grade, type of breast cancer, ER, PR, HER2, Ki-67, p53 protein) was determined by the chi-square test. This test was also used to assess whether the number of NACT cycles had any effect on net tumour size reduction. To identify variables independently related to response to NACT, logistic regression analysis was performed using the SPSS version 23 (SPSS, Inc., Chicago, IL, USA). Social science statistics online software was used to avail Fisher's exact test. Results were considered significant when p was less than 0.05.

3. Result

This was a cross-sectional and observational study that was conducted in the Department of Surgical Oncology of the National Institute of Cancer Research & Hospital (NICRH) from October 2016 to September 2017. The main aim of this study was to observe the clinical and pathological factors as predictors for the responsiveness of NACT in LABC patients. Data regarding the demographic profile, clinical profile, and histopathological profile were collected through a semi-structured data collection sheet. Then, the data were compiled, edited, and decorated in tabular and figure form. The level of significance was determined as 5%. The p-value was set as significant if < 0.05. The observations and results are revealed on the next page. Table 1 shows that out of 100 patients of LABC, 42% and 28% belonged to 41-50 years and 31-40 years age group respectively. The mean age was 44.51±10.77 years, and the age range was 22-73 years. Table 2 shows that out of 100 patients, the highest, 76% had a BMI between 18.5 and 24.99. Subsequently, 13% of patients had it between 25 and 29.99. The mean BMI of the respondents was 23.81±2.36. The BMI range was 17.83-31.13. Table 3 shows the overall epidemiologic characteristics of patients where it was observed that the mean age and BMI of the patients were 44.51±10.77 years (22-73 years) and 23.81±2.36 (17.83-31.13), respectively. 86% of patients were homemakers, 95% were married, and 92% had a history of breastfeeding. Out of 100 patients, 6% had a positive family history of breast cancer. Among 100 patients, 69% never took any form of hormonal contraceptive in their lifetime. Figure 1 shows that out of 100 patients, 87% patients were pre-menopausal, whereas the rest 13% were postmenopausal. Table 4 shows that out of 100 patients, 80% presented with a lump, and 54% had this lump on the left side. 75% of patients manifested regional disease, whereas 25% of patients manifested local disease out of 100 cases, 62% of patients suffered <4 months duration, and subsequently, 35% of patients experienced symptoms from 4-6 months. Only 3% noticed clinical features for more than 6 months. Table 5 shows that out of 100 patients with LABC, there was no such a patient with lump size <2cm, but 13% of patients responded well after NACT as they were found in this group. Initially, 5% of patients belonged to lump size 2-5cm, which was increased to 67% after NACT. On the other hand, 95% of patients had lumps with >5cm in maximum diameter, which was reduced to 20% after NACT. The p-value was found to be significant. Table 6 shows that out of 100 patients with LABC, 76% of patients had pre-NACT palpable axillary lymph nodes, which dropped down to 65% after NACT intervention; on the contrary, 27% of fixed axillary lymph nodes were reduced into 15% fixed axillary lymph nodes. Before NACT, 8% of patients had palpable ipsilateral supraclavicular lymph nodes, which reduced and became 4% after the implementation of NACT. Figure 2 shows that out of 100 LABC patients, 70% received an AC regimen, and 30% received an FEC regimen. Table 7 shows that out of 100 LABC patients' clinical response was observed 77% as PR and 13% as CR. 8% and 2% of patients manifested PD and SD as clinical responses after NACT. Table 8 shows that palpable lymph nodes and NACT types were the statistically significant predictors of responsiveness of NACT. Table 9 shows that age, tumor size, lymphatic and vascular invasion and molecular subtype status were statistically significant predictors of responsiveness of NACT.

Age groups (in years)	Frequency (n)	Percentage (%)			
≤30	15	15.00			
31-40	28	28.00			
41-50	42	42.00			
51-60	10	10.00			
>60	5	5.00			
Mean±SD (in years)	44.51±1	0.77			
Range (in years)	22-73				

Table 1. Distribution of patients according to age (N=100).

BMI category	Frequency (n)	Percentage (%)			
<18.5	8	8.00			
18.5-24.99	76	76.00			
25.00-29.99	13	13.00			
≥30.00	3	3.00			
Mean±SD (kg/m ²)	23.81±2	.36			
Range (kg/m ²)	17.83-31.13				

Table 2. Distribution of patients according to BMI (N=100).

Table 3. Distribution of patients according to epidemiologic characteristics (N=100).

Variables	Mean±SD	Range
Age±SD (in years)	44.51±10.77	22-73
BMI (kg/m ²)	23.81±2.36	17.83-31.13
Variables	Frequency (n)	Percentage (%)
	Occupational status	
Housewife	86	86.00
Service Holders	11	11.00
Student	2	2.00
Business	1	1.00
	Marital status	
Married	95	95.00
Unmarried	5	5.00
	H/O Breast Feeding	
Yes	92	92.00
No	8	8.00
	H/O hormonal contraceptive	
Yes	31	31.00
No	69	69.00
	Family History of Breast cancer	
Present	6	6.00
Absent	94	94.00
Absent	94	94.00

Table 4. Distribution	of patients	according to tumo	r profile ($N=100$).
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Tumor Profile	Frequency (n)	Percentage (%)
	Presenting complaints	
Lump	80	80.00
Lump with ulceration	20	20.00
	Duration of symptoms	
<4 months	62	62.00
4-6 months	35	35.00
>6 months	3	3.00
	Side of involvement	
Left	54	54.00
Right	46	46.00
	Site of involvement	
Local	25	25.00
Regional	75	75.00



Figure 1. *Distribution of patients according to menopausal status (N=100).*

Table 5. Comparison of patients with pre-NACT and post-NACT lump size (N=100).

Lump Size	Pre-NACT]	Post-NACT	P-value	
Lump Size	n	n % n %		%	r-value	
<2 cm	0	0.00	13	13.00		
2-5 cm	5	5.00	67	67.00	<0.00001 ^s	
>5 cm	95	95.00	20	20.00		

Table 6. Comparison of lymph node status of patients between pre-NACT and post-NACT (N=100).

I small reads status		Pre-NACT	1	Post-NACT	D malma				
Lymph node status	n	%	n	0⁄0	P-value				
	Palpable lymph nodes								
Palpable	76	76.00	65	65.00	$0.08^{ m NS}$				
Not palpable	24 24.00 35 35.0		35.00	0.08					
		Fixity of lymph	nodes						
Mobile	73	73.00	85	85.00	0.037 ^s				
Fixed	27	27.00	15	15.00	0.037-				
	Ipsilateral Supraclavicular lymph nodes								
Palpable	8	8.00	4	4.00	0.23 ^{NS}				
Not palpable	92	92.00	96	96.00	0.23				

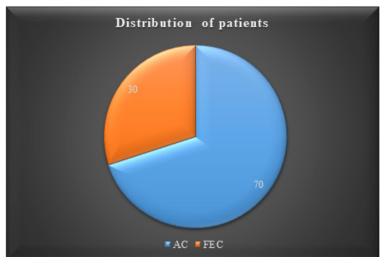


Figure 2. *Distribution of patients according to different NACT regimens (N=100).*

Clinical response	Frequency (n)	Percentage (%)
Complete Response (CR)	13	13.00
Partial Response (PR)	77	77.00
Progressive Disease (PD)	8	8.00
Stable Disease (SD)	2	2.00

Table 7. Distribution of patients according to NACT clinical response (N=100).

Variables	Subgroup	N	CI	R+PR	Univariate	OR	P-value
variables	Subgroup	1	n	(%)	P-value	(95% Cl)	r-value
	≤30	15	13	86.67			
	31-40	28	21	75.00]	1.15	
Age (years)	41-50	42	41	97.60	0.057		0.39 ^{NS}
	51-60	10	10	100.00		(0.81-1.49)	
	>60	5	5	50.00			
Clinical tumor size (cm)	≤ 5	5	5	100.00	0.023	1.25	0.083 ^{NS}
Chinical tullior size (chi)	>5	95	75	78.94	0.023	(0.89-1.73)	0.085***
Mananayaal status	Pre	87	83	95.40	0.791	0.93	0.075 ^{NS}
Menopausal status	Post	13	7	53.84		(0.59-1.33)	0.075
Dolachio izmenia acidos	Negative	24	20	86.95	< 0.001	0.55	0.001 ^s
Palpable lymph nodes	Positive	76	70	90.90	<0.001	(0.39-0.77)	0.001
Chemotherapy type	AC	70	68	97.14	0.023	0.83	0.0208
Chemotherapy type	FEC	30	22	73.33	0.023	(0.23-1.21)	0.029 ^s
	Any positive (ER/PR)	46	43	93.47			
*Molecular subtypes	Both negative (ER/PR)	54	50	92.59	0.893	-	-
	TNBC	34	31	91.17]		
	Others	20	5	25.00			

Table 9. Factors influencing a complete pathological response (N=100).

Variables	<u> </u>		CI	R+PR	Univariate	OR	D 1
	Subgroup	N	n	(%)	P-value	(95% Cl)	P-value
	≤30	15	2	13.33			
-	31-40	28	3	10.71		0.40	
Age (years)	41-50	42	1	2.38	0.039 ^s	0.49 (0.38-0.77)	0.001 ^s
	51-60	10	2	20.00		(0.38-0.77)	
-	>60	5	0	0.00	_		
	≤5	5	1	20.00	0.046 ^s	(0.21.0.90)	0.015 ^s
Clinical tumor size (cm)	>5	95	7	7.36	0.040	(0.31-0.89)	0.015
	Pre	87	6	6.89		-	-
Menopausal status	Post	13	2	15.38	NS		
Lymphatic & vascular	Negative	24	2	8.69	<0.001		
invasion	Positive	76	6	7.79	< 0.001		
	AC	70	4	5.71		4.69	0.031 ^s
Chemotherapy type	FEC	30	3	10.00		(1.13-10.78)	

	Any positive (ER/PR)	46	3	6.52			
*Molecular subtypes	Both negative (ER/PR)	54	1	1.85	0.031 ^s	-	-
	TNBC	34	3	8.82			
	Others	10	1	10.00	1		

4. Discussion

The trendsetters of the oncology field attempted several times to identify predictive factors for chemotherapy response. Unfortunately, the results were conflicting in maximum episodes [9]. Locally advanced breast cancer (LABC) is usually defined as stage III disease. Tumour response to chemotherapy is inversely proportional to tumour size [10]. For this reason, the smaller tumour responds well by getting more shrinkage to allow breast conservation. NACT, if it works well, the plan for immediate reconstruction can also be adopted at the initial stage of LABC management [11]. This prediction of NACT responsiveness is a vital step for a subsequent plan of management. Proper assessment of the tumour to see the response after NACT is very helpful for subsequent planning of surgery [12]. Measurement of the tumour in its maximum diameter, mammography or ultrasonography, depending upon the age of the patients, may provide further information regarding tumour size after NACT [13]. Whether Magnetic Resonance Imaging (MRI) can provide a better correlation with the pathological size remains uncertain, but early results appear promising. Cross et al. have shown that the reduction in tumour enhancement on an MRI scan correlates with the extent of the disease as seen at the pathological examination [14]. However, none of our patients underwent MRI for this assessment after NACT, as the imaging technique is very expensive from our perspective. Breast-sparing radiotherapy for patients who achieved complete clinical response has been proposed by several groups [15]. Accurate estimation of the tumour size after neoadjuvant chemotherapy is crucial for deciding the type and extent of the operation to be performed. This study report of patients with LABC treated by NACT was performed in the surgical oncology department of the National Institute of Cancer Research & Hospital. An analysis was performed to identify the clinic-pathological factors as predictors that are associated with clinical and pathological responses. No survival analysis was performed as it was a short-term study. The mean age of our study respondents was 44.51±10.77 years,

response achieved by initial anthracycline-based NACT with sequential taxane and additional cycles of chemotherapy. In a similar study from India, Parmar et al. noted an increase in pCR rates from 4.3% to 10.5% when 4 or more cycles of NACT were delivered in 1402 women with LABC [23]. Steger et al., in their study, have reported an 11% increase Archives of Oncology and Cancer Therapy V4. I1.2024

which was almost nearest to that of the report of

Tewari et al. (2010), where they stated the mean age

as 47.8 years [16]. A multimodal approach treated the

patients. Brifford et al. reported a highly significant

clinical response in patients with invasive ductal

carcinoma (IDC) [17]. Mathieu et al. and Newman et

al. reported that invasive lobular carcinoma (ILC) is

an independent predictor of ineligibility for BCS after

neoadjuvant chemotherapy compared with IDC [18].

Although all these studies show that ILC patients

are less likely to achieve BCS after neoadjuvant

chemotherapy, they do not address whether the use

of neoadjuvant chemotherapy improves the baseline

BCS rates for ILC patients [18]. The majority of

breast carcinomas in our study are of ductal type. It is

interesting to note that all of our complete responders

were classified as ductal carcinoma, while lobular

carcinoma and inflammatory carcinoma were in the

RCB-III group, which is chemo-resistant. Our finding

is also consistent with a published study showing

that invasive ductal carcinoma is more responsive

to chemotherapy than lobular carcinoma and

inflammatory carcinoma [19]. The overall response

to NACT in this study was 90% (Partial = 77% and

complete = 13%). Several other studies proclaimed

that NACT response to LABC is ranging from 71% to

87% [20]. Interestingly, our results were the highest

from this point of view. Yadav et al., in their study,

reported only 23% of chemo responsiveness to the

NACT [21]. In 2010, Tamer et al. claimed 54.5%

(among the complete response of 3% and the partial

response of 51.5%) response to chemotherapy to the

LABC [22]. In this study, where the majority of the

patients completed chemotherapy prior to surgery, the pCR rate was 36%, which is much higher compared

with other studies from India [23]. Such a higher

rate could be attributed to the consolidation of the

in pCR rates from 7.7% to 18.6% with 6 cycles compared to 3 cycles [24]. The factors which can help the clinician to predict pCR rates reported in various studies include young age, ER/PR negativity, high Ki 67 score, high nuclear grade and smaller tumour size, ductal histology versus pure lobular carcinoma and a number of NACT cycles [25]. The pCR is more likely in hormone receptor-negative, HER-2 overexpressing tumours [26]. The management of patients who progress on NACT has limited options. In our study, a total of 8 patients progressed on NACT. For patients who progress, the regimen can be changed over to non-cross-resistant drugs and observed for a response. For patients with stable disease or local progression, surgery, if feasible, can be offered, or radiotherapy could be considered. In our study of the 8 patients who progressed, 5 had local progression and were offered surgery, and 3 developed systemic disease and surgery was avoided. The reported frequency of progressive disease on NACT is around 3%. The early identification of this subset of patients through frequent clinical assessment may allow for a change of the ineffective regimen to potentially beneficial therapies such as non-cross-resistant chemotherapy, surgery if feasible and radiotherapy [25]. In my study, there was a better response in larger tumours, middle age and ER-negative tumours, as well as in those who were triple negative with a higher rate of pCR. The response was also better with more cycles of chemotherapy. However, there is a bias in this observation as patients who were clinically documented to have an excellent response to chemotherapy in the first 3-4 cycles went ahead to complete the remaining cycles. Most of the tumours were higher grade, and a better response was seen in these tumours. The triple negative subgroup, although it did not demonstrate a clinically superior response to NACT, clearly showed a significantly higher rate of pCR compared to the non-triple negative subtypes. This has been observed in other reports as well, but whether this translated into better survival is not known.

Limitations of the Study

Despite the valuable insights gained from this study on the predictive markers in response to neoadjuvant chemotherapy for locally advanced breast cancer (LABC), several limitations exist. Firstly, the study's cross-sectional design limits the establishment of causal relationships. Longitudinal studies would provide a more comprehensive understanding of the dynamics over time. Secondly, the absence of survival analysis hinders the assessment of longterm treatment outcomes. Additionally, the reliance on self-reported data may introduce recall bias. The study's exclusive focus on a single medical center in Bangladesh may limit the generalizability of findings to broader populations. Furthermore, the lack of utilization of advanced imaging techniques, such as MRI, for response assessment represents a potential gap in evaluating treatment effectiveness. Lastly, the study's duration and sample size may influence the robustness of the results and necessitate cautious interpretation.

5. Conclusion and Recommendations

Breast cancer is the most frequent malignancy among Bangladeshi women. In our perspective, breast cancer usually presents as a locally advanced disease. Different chemotherapy regimens are usually set considering different biological factors of the patients. Based on the findings of this study, it may be concluded that partial response was found to be significant in our patients. However, from the point of view of predictive markers of NACT, palpable lymph nodes, as well as chemotherapy, are the influencing factors for good clinical response. In contrast, age, clinical tumour size, lymphatic and vascular invasion and molecular subtypes are excellent markers for a pathological response.

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Ethical Approval: *The study was approved by the Institutional Ethics Committee.*

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