Ref: Ro J Med Pract. 2024;19(3)
DOI: 10.37897/RJMP.2024.3.8

Assessment of clinical and pathological response to neoadjuvant chemotherapy in breast cancer according to molecular subtypes

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ABSTRACT

Background. *Breast cancer (BC) is the commonest tumor in women. It is the leading malignancy in world, and representing an emerging oncologic issue in all countries. In Iraq, BC cases reached 7246 in 2021by Iraqi Cancer Registry reports.*

Objectives. *The study conducted for assessment the clinical and pathological responses to neoadjuvant chemotherapy in BC among molecular subtypes and for description the clinico-pathologic features, and patterns of BC according to molecular subtypes.*

Methods. *A prospective study of 60 females with breast cancer histologically confirmed were enrolled. All women received neoadjuvant chemotherapy. Then all patients underwent definitive surgery including MRM+AC or BCS+AC. The patients' demographic, the pathologic and molecular subtypes date of the primary tumor were recorded.*

Results. *The mostly distributed age group was belong to group 46-55 yrs in 22, 36.7%. The mean age was 49.7±10.8 yrs. The IDC represented the most common histopathological types of BC. The most of cases seen in upper-outer quadrant (UOQ). The results post-chemotherapy as followed: ypTx stage reported in 32 (53.3%), ypT1 in 15 (25.0%), ypT2 in 10 (16.7%) and ypT3 in 3 (5.0%). ypN0 stage in 40 patients (66.7%), ypN1 in 11 (18.3%), ypN2 in 6 (10.0%), and ypN3 in 3 (5.0%). There was a high statistical difference between cT and ypT in pre and post-chemotherapy (P<0.0001), between cN and ypN in pre and post-chemotherapy (P=0.001) and between M and ypM in pre and post-chemotherapy (P=0.002). The mass location (P=0.005) and tumor size (P = 0.011) had significantly impacted on BC responses post NACT. 18(30.0%) had clinical complete response (cCR), 32 women (53.3%) had partial response (cPR), six cases (10.0%) had stable disease, and four cases (6.7%) had progressive disease. The cCR was better seen in T1 (77.8%) than T2 (22.2%), with statistical significant difference (P=0.002). The cCR was better seen in N0 (61.1%) than N1 (38.9%), with a high statistical significant difference (P<0.0001).*

Conclusions. *The commonest age breast cancer is four to five decade. The IDC and mass situated at UOQ are the most common features of BC. Approximately, 30.0% of women have clinical complete response (cCR), 53.3% have partial response (cPR), 10.0% have stable disease, and 6.7% have progressive disease post NACT. The ER positive, PR positive, and HER2neu negative are the mostly frequent subtype recorded in this study. The cCR is better seen in T1 and N0 stages. ER+ and PR+ are more reported after NACT whereas HER2neu- is more post NACT.*

Keywords: breast cancer, progressive disease, stable disease, upper-outer quadrant, neoadjuvant chemotherapy, clinical complete response

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Article History:
Received: 1 July 2024
Accepted: 5 September 2024

INTRODUCTION

Breast cancer (BC) is the commonest tumor in women. It is the leading malignancy in the world. Annually, more than 500 thousands women dying from BC [1]. In Iraq, BC cases reached 7246 in 2021by Iraqi Cancer Registry reports [2]. BC has a heterogeneous collection with various histo pathologically subsets, clinical features, responses to management, and prognosis [3]. Surgical oncologists, radiation oncologists, pathologists, radiologists, reconstructive surgeons, and supportive care staff are all essential members of the interdisciplinary team that provides BC therapy [1,4-6]. Considerations of lymph node metastasis, age at diagnosis, tumor grade and histology, primary tumor size, HR, and Her2neu status are among the clinical and histological characteristics that hold predictive value [7-9]. Histopathologic categorization according to morphologic characteristics resulted from these heterogeneities. The AJC has identified fifteen separate histopathologic types of cancer [9]. By 2020, the Iraqi Cancer Registry (ICR) maintained by the Ministry of Health had documented over 7,000 cases of BC in women. A total of 18.96% of cases were reported, with a morbidity rate of 11.53% [2,5]. Recently, in 2021, GLOBOCAN published the Global Cancer Observatory reports. About 7,515 new cases of BC recorded in Iraq, and about 3,019 deaths [10,11]. The update of Iraqi Board cancer registry in 2023, reported more than 7.5 thousands cases of BC (>30% of all cancer types) in Iraq [5].

Globally, an update published by GLOBOCAN, found that female BC account for 2,261,419 new cases and about 684,996 new deaths, it is ranked in level one in all cancer types list [12]. According to the National Surgical Adjuvant Breast Project (NSABP) B-06 trial, participants whose tumors tested positive for either ER or PR had a slightly better prognosis than those whose malignancies tested negative for both ER and PR [13], where ER and PR measured by biochemical methods. ER and PR measured by current IHC techniques represent very strong predictive factors for response to hormone therapy rather than being strong prognostic factors for survival. The main reasons for the inaccuracy in 20% of the current IHC ER and PR determinations include differences in pre-analytical factors, positivity thresholds, and interpretation criteria, which might lead to false negative or positive results [9,13].

Systemic treatment prior to a decisive procedure is known as neoadjuvant chemotherapy (NAC). Historically, NAC has only been performed on patients with locally advanced or inoperable BC. Its main goal was to down-stage the tumor size so that BCS could be performed, and in certain situations, patients who were against lengthy surgery might have axillary dissection avoided. But now NAC can also help in cases of operable, early-stage breast cancer. Consequently, NAC lessens postoperative problems such lymphedema and allows for better esthetic results [14].

No significant difference in long-term results was seen between adjuvant chemotherapy and NAC in clinical trials comparing the two methods for early-stage and locally advanced BC. The in vivo validation model provided by NAC allows for the testing of treatment efficacy, which is important because chemo-sensitivity levels vary among tumor types and individuals, impacting long-term outcomes. In triple-negative breast cancer (TNBC) and HER2-positive breast cancers, the surrogate endpoint, chemotherapeutic response, is a powerful predictor of recurrence risk [15–17]. Widespread use of NAC has been caused by the benefits [14].

Molecular subtypes of breast cancer were the focus of this study, which aimed to describe the clinico-pathologic features and patterns of BC and evaluate the clinical and pathological responses to neoadjuvant chemotherapy in BC.

METHODS

Study design and setting

Sixty women who had breast cancer that had been verified histologically participated in the trial. Neoadjuvant chemotherapy was administered to all survivors. After that, every single patient had either BCS+AC or MRM+axillary lymph node dissection (AC) as their final surgical procedure. We documented the demographics of the patients, as well as the pathologic and molecular subtypes of the underlying tumor. The research took place from December 2023 to April 2024 at the following locations: Baghdad Radiotherapy and Nuclear Medicine Center, Baghdad Medical City Complex, Baghdad, Iraq; Baghdad Oncology Teaching Hospital; and National Cancer Center.

Inclusion criteria

- All untreated female with primary BC.
- Women aged 18-70 years.
- Oligo-metastasis.

Exclusion criteria

- Women not willing.
- Benign breast diseases.
- Male BC.
- Metastasis BC (multiple).

Data collection

All of the surgery specimens were sent for the standard pathology report. All information about ER, PR and HER2 status. In our retrospective review of the clinico-

pathological records, we took the following factors into account: age, co-morbidities (DM, HT, etc.), histologic type, laterality, tumor size, M stage, estrogen receptor, progesterone receptor, HER-2 negative, chemotherapy, surgery, ypT stage, ypN stage, and HR data post-pathological responses. Conventional radiographs, ultrasound, mammogram, computed tomography, or magnetic resonance imaging (PET scan) were used to determine the clinical stage of BC, which was then confirmed by tissue biopsy.

Ethical considerations

Before patients could take part in this trial, they had to give their written informed consent. All patients' parents gave their informed consent so the study could follow the guidelines laid out in the Declaration of Helsinki and its subsequent revisions. The study (#No.1674 dated 26/12/2023) was approved by the Institutional Ethical Board of the Department of Surgery, College of Medicine, University of Baghdad.

Groups*

The tumors of the luminal tissues were categorized as luminal A (ER+ and PR+/HER2−, Nottingham grades I-II) and luminal B (ER+and/or PR+/HER2−, grade III or ER+and/or PR+/HER2+). Positive for HER2; negative for ER and PR. There was no additional sub-classification of tumors having a triple-negative phenotype, even if this subgroup does constitute basal-like malignancies. Tumors were considered triple-negative (basal-like) if they were ER-negative, PR-negative, and HER2 negative.

Study conclusions

The rate of pCR according to molecular subtypes was the main endpoint. The pathological complete remission (pCR), is the absence of any invasive breast or axillary cancer following neoadjuvant treatment [48].

Statistical analysis

All analyses were conducted by using SPSS version 25.0 for Windows (SPSS Inc., Chicago, Illinois, USA). Qualitative data consist of numbers and percentages were measured. Mean and SD for quantitative data also calculated. A two-sided P value of 0.05 or less and 95% CI were considered statistically significant for Pearson chi-square, and student paired t-test were used to analyze the differences between the variables.

RESULTS

Patients baseline characters

The mostly distributed age group was belong to group 46-55 yrs in 22 cases (36.7%), followed by group 56-65 yrs in 19 cases (31.7%). The mean age was 49.7±10.8 yrs (median= 50 yrs; range 27-68 yrs). According to comorbidities, data recorded 8 (13.3%) pacients suffered from HT, 4 (6.7%) patients with DM+HT, two cases with thyroid disorders, and one woman with other primary (Table 1).

TABLE 1. *Baseline characters distribution in women with BC (n=60)*

Characteristics		n (%)
Age (years)	26-35	9 (15.0)
	36-45	8 (13.3)
	46-55	22 (36.7)
	56-65	19 (31.7)
	>65	2 (3.3)
Comorbidity	DM	1 (1.7)
	HT	8 (13.3)
	DM+HT	4 (6.7)
	Thyroid disease	2 (3.3)
	Other cancer	1 (1.7)
	Absent	44 (73.3)

DM – diabetes, HT – hypertension

Tumor baseline characters

The right sided BC was reported in 34 (56.7%) of women while left sided was found in 43.3%. The IDC represented the most common histopathological types of BC in 59(98.3%) of patients. In relation to location of tumor, most of cases seen in upper-outer quadrant (UOQ) (34, 56.7%).

The size of tumor (0.5-2 cm) and (2-5) was found in 29(48.3) of patients for each. The cTx stage was found 2(3.3%), cT1 in 28 (46.7%), and cT2 in 21 (35.0%). The cT3 recorded in four cases. The cT4 recorded in five cases. Two cases showed oligo-metastasis. The cN0 recorded in four cases, cN1 in 52 (86.7%), and two cases in cN2 and cN3. 28/60 cases either received AC+T or TCHP chemotherapies. One received AC, two received AC+TC and one received TCH. Most patients under went MRM+ALND (65.0%) whereas 28.3% treated by BCS+ALND and 6.7% by WLE+ALND. The results post-chemotherapy as followed: ypTx stage reported in 32 (53.3%), ypT1 in 15(25.0%), ypT2 in 10 (16.7%) and ypT3 in 3 (5.0%). ypN0 stage in 40 patients (66.7%), ypN1 in 11 (18.3%), ypN2 in 6 (10.0%), and ypN3 in 3 (5.0%), as shown in (Table 2).

IDC stands for invasive ductal carcinoma, ILC stands for invasive lobular carcinoma, IOQ refers to the inferior outer quadrant, IUQ refers to the inferior upper quadrant, LIQ refers to the lower-inner quadrant, LOQ refers to the lower-outer quadrant, UOQ refers to the upper-outer quadrant, AC refers to doxorubicin hydrochloride (Adriamycin) and cyclophosphamide, T refers to Taxol (Paclitaxel), TC refers to Taxotere and cyclophosphamide, H refers to Herceptin, TCHP refers to

TABLE 2. *Tumors characters distribution in women with BC (n=60)*

Characteristics		n (%)
Laterality	Right	34 (56.7)
	Left	26 (43.3)
Histopathology	IDC	59 (98.3)
	ILC	1 (1.7)
Location	IOQ	1 (1.7)
	IUQ	5 (8.3)
	LIQ	4 (6.7)
	LOQ	11 (18.3)
	UOQ	34 (56.7)
	Retro-areolar	3 (5.0)
	Sub-areolar	2 (3.3)
Tumor size (cm)	0.5-2	29 (48.3)
	2-5	29 (48.3)
	>5	2 (3.3)
cT	x	2 (3.3)
	1	28 (46.7)
	2	21 (35.0)
	3	4 (6.7)
	4	5 (8.3)
cN	0	4 (6.7)
	1	52 (86.7)
	2	2 (3.3)
	3	2 (3.3)
M	0	58 (96.7)
	1	2 (3.3)
Chemotherapy	AC	1 (1.7)
	AC+T	28 (46.7)
	AC+TC	2 (3.3)
	TCH	1 (1.7)
	TCHP	28 (46.7)
Surgery	BCS+ALND	17 (28.3)
	MRM+ ALND	39 (65.0)
	WLE+ ALND	4 (6.7)
ypT	1	47 (78.3)
	2	10 (16.7)
	3	3 (5.0)
ypN	0	40 (66.7)
	1	11 (18.3)
	2	6 (10.0)
	3	3 (5.0)
ypM	0	60 (100.0)

docetaxel, carboplatin, trastuzumab and pertuzumab, BCS refers to Breast-conserving surgery, ALND refers to axillary LN dissection, MRM refers to modified radical mastectomy, and WLE refers to wide local excision.

Comparison between BC stages pre and post chemotherapy

As shown in Table 3, there was a high statistical difference between cT and ypT in pre and post-chemotherapy (t=39.263, P<0.0001).

TABLE 3. *Comparison between T stages pre and post chemotherapy*

T stage		ypT			Total
		1	2	3	
cT	x	2	0	0	2
	1	28	0	0	28
	2	17	4	0	21
	3	0	4	0	4
	4	0	2	3	5
	Total	47	10	3	60

Paired t-test =39.263, P<0.0001

As shown in table (4), there was a high statistical difference between cN and ypN in pre and post-chemotherapy (t=11.589, P=0.001).

TABLE 4. *Comparison between N stages pre and post chemotherapy*

N stage		ypN				Total
		0	1	2	3	
cN	0	4	0	0	0	4
	1	32	11	6	3	52
	2	2	0	0	0	2
	3	2	0	0	0	2
	Total	40	11	6	3	60

Paired t-test =11.589, P=0.001

As shown in table (5), there was a statistical difference between M and ypM in pre and post-chemotherapy (t-test =9.154, P=0.002).

TABLE 5. *Comparison between M stages pre and post chemotherapy*

M stage		ypM		Total
		0	1	
M	0	58	0	58
	1	2	0	2
	Total	60	0	60

Paired t-test =9.154, P=0.002

Comparison between BC hormonal receptors pre and post chemotherapy

As shown in Table 6, there was a highly statistical difference between ER in pre and post-chemotherapy (X^2=52.2, P<0.0001).

TABLE 6. *Comparison between ER pre and post chemotherapy*

ER		Post		Total
		Positive	Negative	
Pre	Positive	31	1	32
	Negative	1	27	28
	Total	32	28	60

Pearson Chi-Square= 52.2, df=1, P<0.0001

As shown in table (7), there was a highly statistical difference between PR in pre and post-chemotherapy (X2=52.4, P<0.0001).

TABLE 7. *Comparison between ER pre and post chemotherapy*

PR		Post		Total
		Positive	Negative	
Pre	Positive	33	2	35
	Negative	0	25	25
	Total	33	27	60

Pearson Chi-Square= 52.4, df=1, P<0.0001

As shown in table (8), there was a highly statistical difference between HER2neu in pre and post-chemotherapy (X^2=56.1, P<0.0001).

TABLE 8. *Comparison between ER pre and post chemotherapy*

HER2neu		Post		Total
		Positive	Negative	
Pre	Positive	29	0	29
	Negative	1	30	31
	Total	30	30	60

Pearson Chi-Square= 56.1, df=1, P<0.0001

OUTCOME

Regarding clinical response rates, among 60 females, 18(30.0%) had clinical complete response (cCR), 32 women (53.3%) had partial response (cPR), six cases (10.0%) had stable disease, and four cases (6.7%) had progressive disease (Table 9).

TABLE 9. *Responses rates of women with BC (n=60).*

Response	n (%)
cCR	18 (30.0)
cPR	32 (53.3)
Stable disease	6 (10.0)
Progressive disease	4 (6.7)

cCR – clinical complete response, cPR – partial response

Regarding responses post chemotherapy, the cCR rate was good in those aged >50 yrs, women without co-morbidities, patients with right IDC BC, those the mass located at sites other than UOQ, tumor size less than 5 cm, women received [AC, AC+T, AC+TC] protocols and those with ER+, PR+ and HER2 neu-.

The cPR seen more in those aged <50 yrs, women without co-morbidities, patients with right IDC BC, those with mass located at UOQ, tumor size less than

TABLE 10. *Post-chemotherapy response rates according study variables (n=60)*

Variable		cCR (n=18)	cPR (n=32)	Stable disease (n=6)	Progressive disease (n=4)	P value
		n (%)				
Age	<50 yrs	8 (44.4)	24 (75)	4 (66.7)	3 (75)	0.17
	>50 yrs	10 (55.6)	8 (25)	2 (33.3)	1 (25)	
Co-mobidity	Yes	6 (33.3)	8 (25)	2 (33.3)	0	0.92
	No	12 (66.7)	24 (75)	4 (66.7)	4 (100)	
Laterality	Right	12 (66.7)	18 (56.3)	3 (50)	1 (25)	0.47
	Left	6 (33.3)	14 (43.7)	3 (50)	3 (75)	
Histopathology	IDC	18 (100)	31 (96.9)	6 (100)	4 (100)	0.28
	ILC	0	1 (3.1)	0	0	
Location	UOQ	8 (44.4)	25 (78.1)	1 (16.7)	0	0.005
	Others	10 (55.6)	7 (21.9)	5 (83.3)	4 (100)	
Tumor size	<5	18 (100)	32 (100)	6 (100)	2 (50)	0.011
	>5	0	0	0	2 (50)	
Chemotherapy	AC, AC+T, AC+TC	14 (77.8)	14 (43.7)	3 (50)	0	0.07
	TCH, TCHP	4 (22.2)	18 (56.3)	3 (50)	4 (100)	
ER	Positive	12 (66.7)	20 (62.5)	0	0	0.08
	Negative	6 (33.3)	12 (37.5)	6 (100)	4 (100)	
PR	Positive	13 (72.2)	20 (62.5)	0	0	0.72
	Negative	5 (27.8)	12 (37.5)	6 (100)	4 (100)	
HER2neu	Positive	6 (33.3)	16 (50)	5 (83.3)	3 (75)	0.13
	Negative	12 (66.7)	16 (50)	1 (16.7)	1 (25)	

IDC – Invasive ductal carcinoma, UOQ – upper-outer quadrant, AC – doxorubicin hydrochloride (Adriamycin) and cyclophosphamide, T – Taxol (Paclitaxel), TC – Taxotere and cyclophosphamide, H – Herceptin, TCHP – docetaxel, carboplatin, trastuzumab and pertuzumab, ER – Estrogen receptor, PR – Progesterone receptor, HER2neu – human epidermal growth factor receptor 2, cPR – clinical partial response, cCR – clinical complete response

5 cm, women received [TCH, TCHP] protocols and those with ER+ and PR+.

The stable disease recorded more in those aged <50 yrs, women without co-morbidities, patients with IDC BC, those with mass located other than UOQ, tumor size less than 5 cm and those with ER-, PR-, and HER2 neu+.

The progression BC found more in younger than 50 yrs, women without co-morbidities, patients with left IDC BC, those with mass located other than UOQ, women received [TCH, TCHP] protocols and those with ER-, PR-, and HER2 neu+.

Table 10 showed that only mass location (P=0.005) and tumor size (P=0.011) had significantly impacted on BC responses post NACT.

In Table 11, shown post-chemotherapy response rate in relation to T stage. The cCR was better seen in T1 (77.8%) than T2 (22.2%). In relation to cPR, the majority of cases (90.6%) were belonged to T1 and only three cases were T2. The stable disease was reported in four cases of T1 and two cases of T2. The disease progressed in 3(75%) cases of T3, with statistical significant difference (P=0.002).

TABLE 11. *Post- chemotherapy response rate in relation to T stage (n=60)*

ypT	cCR (n=18)	cPR (n=32)	Stable disease (n=6)	Progressive disease (n=4)	P value
	n (%)				
1	14 (77.8)	29 (90.6)	4 (66.7)	0	0.002
2	4 (22.2)	3 (9.4)	2 (33.3)	1 (25)	
3	0	0	0	3 (75)	

In Table 12 shown Post- chemotherapy response rate in relation to N stage. The cCR was better seen in N0 (61.1%) than N1 (38.9%). In relation to cPR, the majority of cases (90.6%) were belonged to N0 and only three cases were N1. The stable disease was reported in four cases of N2. The disease progressed in 2(50%) cases foe eachN2 and N3, with a high statistical significant difference (P<0.0001).

TABLE 12. *Post-chemotherapy response rate in relation to N stage (n=60)*

ypN	cCR (n=18)	cPR (n=32)	Stable disease (n=6)	Progressive disease (n=4)	P value
	n (%)				
0	11 (61.1)	29 (90.6)	0	0	<0.0001
1	7 (38.9)	3 (9.4)	1 (16.7)	0	
2	0	0	4 (66.7)	2 (50)	
3	0	0	1 (16.7)	2 (50)	

DISCUSSION

In this study, 60 Iraqi women with mean age of 49.7±10.8 yrs (median= 50 yrs; range 27-68 yrs). Off 60 cases, 8 (13.3%) suffered from HT, 4 (6.7%) patients with DM+HT, two cases with thyroid disorders, and one woman with other primary. The BC characters of sample are right sided tumor in 34 (56.7%) while left sided in 43.3%, IDC represented the most common histopathological types in 59 (98.3%), and most of masses seen in UOQ (34, 56.7%). In addition, the size of tumor (0.5-5) was found in 48 patients, the cT1 stage was prevalent 28 (46.7%), two cases showed oligo-metastasis, and cN1 recorded in 52 (86.7%). In Iraq, Al-Naqqash et al. [18,19], Al-Alwan et al. [20] and Al-Rawaq [21] are seemly reported similar findings. However, our findings different from that results recorded in Goldhirsch et al. [22].

In the present study, 28/60 cases either received AC+T or TCHP chemotherapies. Most patients under went MRM+ALND (65.0%). The results post-chemotherapy as followed: ypT1 in 47 (78.3%), ypT2 in 10 patients (16.7%) and ypT3 in 3 (5.0%). The ypN0 stage in 40 patients (66.7%), ypN1 in 11 (18.3%), ypN2 in 6 (10.0%), and ypN3 in 3 (5.0%). These results are dissimilar with Al-Naqqash's study [18], but agree with Al-Sarraf [23], and El-Fatemi and Chahbounil, 2012 [24].

Tang and co-authors [25], studied 300 Chinese women retrospectively. The NACT protocols included 4-6 cycles of TAC regimen, 2-5 cycles of a FAC regimen, ACT regimen, four cycles of AT regimen, 4 cycles of TCBP regimen. The study found a strong association between clinical response and LN status. Additionally, there were no notable variations in response according on age, tumor size, menstruation status, chemotherapy frequency, Ki67 value, and molecular subtypes.

The present study found a significant statistical difference between cT and ypT before and after chemotherapy (P<0.0001). Similarly, there was a significant statistical difference between cN and ypN before and after chemotherapy (P=0.001). Additionally, there was a statistical difference between M and ypM before and after chemotherapy (P=0.002). The original reports of the link between the pCR to neoadjuvant chemotherapy and outcomes in the landmark National Surgical Adjuvant Breast and Bowel Project B-18 and B-27 trials were made by Mieog et al. [26] and Kong et al. [27]. These findings agree with those reports. Also, Tang et al. [25], Caudle et al. [28] and Tee et al. [29] showed the same results. This phenomenon was highlighted in luminal B. BC with luminal B may potentially contribute to axillary LN conservation and sentinel LN biopsy after neoadjuvant chemotherapy [25].

In India, Sharma et al. [30] conducted a prospective and retrospective observational study included 31

women. All patients received NACT 4 cycles of ACT. The median age was 49 yrs, right BC more than left, >5 cm tumor size in 93.54%, all LN positive, IDC prevalent, and the upper outer quadrant (58.06%) was the most commonly involved quadrants, which are the same findings in our study.

In the present study, there was a highly statistical difference between ER in pre and post-chemotherapy (P<0.0001), between PR in pre and post-chemotherapy (P<0.0001), and between HER2neu in pre and post-chemotherapy (P<0.0001). These data supported by Tang et al. [25], Sharma et al. [30] and Kunnuru et al. [31]. Tang et al. [25] calculated the univariate and multivariate tests of Cox regression analysis which showed that PR/CR and pCR are not the factors influencing prognosis, these differ from the findings of Romero et al. [32], Asaoka et al. [33], and Cortazar et al [34]. But, it similar to those reported by Korn et al. [35], Chen et al. [36] and Berruti et al. [37].

In the present study, among 60 females, 18(30.0%) had clinical complete response (cCR), 32 women (53.3%) had partial response (cPR), six cases (10.0%) had stable disease, and four cases (6.7%) had progressive disease. The cCR rate was good in women aged >50 yrs, without co-morbidities, right IDC BC, the mass located at sites other than UOQ, tumor size <5 cm, received [AC, AC+T, AC+TC] protocols and ER+, PR+ and HER2 neu-. The cPR seen more in those aged <50 yrs, without co-morbidities, right IDC BC, mass located at UOQ, tumor size <5 cm, received [TCH, TCHP] protocols and ER+ and PR+. The stable disease recorded more in those aged <50 yrs, without co-morbidities, IDC BC, mass located other than UOQ, tumor size <5 cm and ER-, PR-, and HER2 neu+. People under the age of 50 who do not have any other health problems, who have a mass outside of the UOQ, who have undergone [TCH, TCHP] protocols, and who test negative for ER, PR, and HER2 are more likely to have a progression of BC. Compared to what Sharma et al. reported, these results were over double. A clinical response was observed in 83.87% of the individuals that underwent NACT, and the cCR was detected in 22.58% of those cases, according to [30]. With a p-value less than 0.0001, 51.61 percent of cases turned clinically LN negative after NACT, and 67.74 percent saw clinical down staging. Fifty percent of HER2 overexpression cases, twenty-five percent of TNBC cases, and no cCR in luminal B subtype cases were seen. In 19.35% of the instances that were included, the pCR was seen. In luminal A, 80%, 62.50%, and 37.50% of the TNBC and HER2 overexpression subtypes, respectively, cPR was seen.

Also, our study showed the cCR was better seen in T1 (77.8%) than T2 (22.2%). In relation to cPR, the majority of cases (90.6%) were belonged to T1 and only three cases were T2. The stable disease was reported in four cases of T1 and two cases of T2. The disease progressed in 3(75%) cases of T3, with statistical significant difference (P=0.002). The cCR was better seen in N0 (61.1%) than N1 (38.9%). In relation to cPR, the majority of cases (90.6%) were belonged to N0 and only three cases were N1. The stable disease was reported in four cases of N2. The disease progressed in 2 (50%) cases foe each N2 and N3, with a high statistical significant difference (P<0.0001). The findings of our study align with those of Kunnuru et al. [31], who reported that out of the total number of patients, 16 (26.6%) had complete clinical response (cCR), 30 (50%) achieved partial clinical response (cPR), eight (13.3%) maintained stable disease, and six (10%) saw illness progression. Furthermore, after undergoing chemotherapy, a total of 16 patients (26.7%) achieved complete remission (T0). Out of the 32 patients (53.3%) with pre-chemotherapy T4 illness, only eight patients (13.3%) still had T4 stage after chemotherapy (P<0.05). Furthermore, 12 patients (20%) were diagnosed with N2 stage disease prior to receiving chemotherapy. This number decreased to four patients (6.7%) after undergoing chemotherapy (P<0.05). Patients with ER-positive tumors had a higher complete clinical response (cCR) rate compared to patients with ER-negative tumors when treated with neoadjuvant chemotherapy (NACT) (P <0.05). However, there was no significant disparity in PR status and HER2-neu status when considering the response rate following NACT.

Gedam et al. [38] and Siddhartha and Kanchana [39] supported our findings in their studies regarding cCR and cPR. In their study, Gentile et al. [40] found that 48% of individuals with HER2 overexpression and 23% of cases with TNBC achieved pCR. Luangdilok et al. [41] and Subbiah et al. [42] demonstrated that HER2 overexpression and TNBC subtypes had a higher rate of pathological complete response (pCR) in comparison to luminal subtypes.

The variations in response to chemotherapy across different subtypes of breast cancer, such as TNBC and HER2 overexpression BC, can be attributed to the elevated expression of the proliferative cluster of genes [30]. In addition, TNBC is characterized by a lack of estrogen and progesterone receptors (ER/PR) and research indicates that the absence of these hormone receptors is strongly correlated with a higher probability of achieving a pathological complete response (pCR) to neoadjuvant chemotherapy (NACT) [43-45].

According to Sharma and colleagues [30], they found that more than 80% of cases showed a decrease in tumor size, which led to complete clinical response (cCR) and partial clinical response (cPR). Pathological regression of the invasive tumor was observed in 20% of instances. The evaluation of the reaction of molecular subtypes to neoadjuvant chemotherapy (NACT) in-

dicates that HER2 overexpression and triple-negative breast cancer (TNBC) exhibit superior clinicopathological response compared to luminal subtypes. Molecular subtype determination is useful for determining chemotherapy treatments. Neoadjuvant chemotherapy (NACT) leads to the reduction of tumor size, which in turn aids in completing complete removal of the tumor during surgery and eliminates small cancer cells that have spread to other parts of the body. This decreases the likelihood of the tumor coming back and reduces the associated risks and complications.

In the present study, there was a highly statistical difference between ER+ and PR+ in pre and post-chemotherapy and between HER2neu(-). Kunnuru et al. [31] said that the utilize of NACT in BC is very effective. The researchers discovered that the total percentage of complete and partial clinical responses was 76.6%. Breaking down the response rates by component, they found: After three rounds of chemotherapy, the following percentages hold: 94% in ER-positive tumors, 50% in ER-negative tumors, 83.8% in PR-positive tumors, 68.8% in PR-negative tumors, 84.2% in HER2-positive tumors, and 87.8% in HER2-negative tumors. In a study conducted by Olfaa et al. [46], the clinical response rate was determined using univariate analysis. The results showed that 63% of tumors with ER-positive, 84% with ER-negative, 59% with PR-positive, 62% with PR-negative, 64% with HER2-positive, and 62% with HER 2 negative tumors. Regarding patients' HER2-neu status, Resende et al. [47] found no correlation.

According to Kunnuru et al. [31], NACT can reduce the visibility of operable cancers' main tumors and axillary metastases. In cases with locally advanced cancer, the combination of Taxol plus chemotherapy based on anthracyclines produces favorable clinical and pathological outcomes. Pathological response is favorable in individuals with triple-negative and Luminal A tumors, however clinical response differs among tumor subtypes. The best approach to identify the factors that predict a patient's response to chemotherapy is to compare molecular subtypes with the response.

Prospective studies are needed worldwide to find out whether we can predict overall and disease-free survival from the full pathologic response, and in 2023, multiple clinical practice authors brought up the idea that BC subtyping by molecular types is one way to approach evaluating the NACT [48–52]. The question of whether PR and pCR to neoadjuvant chemotherapy could transfer into long-term prognosis advantages was also investigated by Tang et al. [25]. No statistically significant changes were found in the pathological response between the pCR and non-pCR groups when comparing them throughout a 5-year OS period. There was no evidence that cCR and cPR could be used as prognostic indicators in either the univariate or multivariate analyses. Both the clinical response group and the pathological response group did not show a statistically significant difference in cancer recurrence [25].

In their study, Alba et al. [53] found that a Ki67 proliferation index higher than 50% could potentially predict pCR to NACT. They also noted that cell proliferation is closely linked to chemosensitivity. Factors that affect prognosis over time were shown by Baulies et al. [54]. The subtype of malignancy and the success rate of pCR determine the intervals between recurrences in BC patients treated with NACT. Patients with more aggressive biological behavior tend to have worse first-year outcomes, and patients with HR+ BC continue to be at risk for distant recurrence for a considerable amount of time. This group's emphasis was on the biological aspects of breast cancer and its effects, as opposed to the association between chemotherapy and survival rates [25].

Most research concentrated on chemotherapy regimens for HER-2+ and TNBC, according to meta-analyses by Schettini et al. [55] and Li et al. [56]. There is a lack of literature that compares the clinical response and pathological response across different regimen types or that compares these outcomes across different subtypes.

No statistically significant variations in survival were seen among the various treatment regimens, as Tang et al. [25] showed. Results from the Fisher's exact test were almost statistically significant in the group of patients with luminal A group BC. Luminal B, HER-2+, and TNBC-treated patients did not differ significantly with respect to cancer recurrence.

CONCLUSION

The commonest age breast cancer is four to five decade. The IDC and mass situated at UOQ are the most common features of BC. Approximately, 30.0% of women have clinical complete response (cCR), 53.3% have partial response (cPR), 10.0% have stable disease, and 6.7% have progressive disease post NACT. The ER positive, PR positive, and HER2neu negative are the mostly frequent subtype recorded in this study. The cCR is better seen in T1 and N0 stages. ER+ and PR+ are more reported after NACT whereas HER2neu- is more post NACT.

Conflict of interest: none declared
Financial support: none declared

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