



## Value of Hormone Receptor Status in Patients with Locally Advanced Breast Cancer as Regard the Response to Neoadjuvant Chemotherapy

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**Abstract: Background:** To investigate the value of hormone receipt or expression status in patients with locally advanced breast cancer as regard the response to neoadjuvant chemotherapy. **Methods:** 72 stage II-III breast cancer patients treated with neoadjuvant chemotherapy were prospectively studied. Data of patients is divided into two groups based on the hormone receptor expression status: Group A, patients with HR-positive; Group B, patients with HR negative. **Results:** Among over all 72 patients received NAC; their age ranged from 31-68ys, and 42.86% were postmenopausal. Complete response (CR) was achieved in 12 patients (16.7%), it reached 23% in HR -ve patients and 13% of HR +ve patients. Most of patients underwent MRM; 69.57%, and 61.54% in HR +ve and HR -ve group respectively. In group A (46 patients), 32 patients underwent MRM (69.57%), 14 patients underwent CBS (30.43%) and pCR was achieved in 4 patients (8.6%). While, in group B (26 patients), 16 patients underwent MRM (61.54%), 10 patients underwent CBS (38.46%) and pCR was achieved in 5 patients (19.2%). **Conclusions:** patients with hormone receptor negative breast cancer have a better response to neoadjuvant chemotherapy and more liable to achieve complete response (CR) than patients with HR +ve breast cancer.

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**Keywords:** Breast cancer, neoadjuvant chemotherapy, hormone receptor, pathological complete response.

### 1. Introduction

Breast cancer ranks second in cancers affecting Egyptians (15.4%), and the commonest malignancy among Egyptian females (32%). The median age at diagnosis is one decade younger than other western countries. Patients usually presents with advanced disease.<sup>1</sup>

Locally advanced breast cancer (LABC) represents as a heterogeneous group of breast cancer considered to be an advanced disease due to either; its size ( $\geq 5$  cm in size, T3N0 T3N1, or N2. or its location that may make them inoperable (ex. insufficient skin flaps for closure).<sup>2</sup>

Total mastectomy was the only surgical treatment for operable LABC, till the evolving of the era of down staging by NAC. it also targets and controls micrometastasis.<sup>3</sup>

The sequence of chemotherapy to surgery (neoadjuvant vs. adjuvant) does not affect the overall survival, neoadjuvant chemotherapy (NAC) is given to patients with an inoperable LABC to improve the chances of R0 resection and gives better surgical options like breast conservation instead of MRM. it

also allows the assessment of the response to systemic treatment *in vivo* to evaluate its efficacy<sup>4</sup>.

According to immunohistochemistry test breast cancers can be classified based on the hormone receptor HR status; (estrogen receptor ER and progesterone receptor PR) and human epidermal growth factor receptor 2 (Her 2) receptor expressions. The effect of NAC varies according to the intrinsic subtype of tumors. Patients with HER2 receptor positive and triple-negative breast cancer (TNBC) have better responses and higher pathologic complete response (pCR) rates, while HR-positive breast cancer is known to have better prognosis despite its lower sensitivity to chemotherapy<sup>5</sup>. The prediction of the clinical response depends on the tumor biology and it is only achieved in 20% to 30% of patients.<sup>6</sup>

According to the response to NAC; tumors that achieve a pathological complete response (pCR) have shown to have lower recurrence rates in comparison to those with partial responses<sup>6</sup>.

One of the potential advantages of neoadjuvant chemotherapy is decreasing the size of the primary tumor, making BCT convenient. published studies

concluded that; around 23%–32% of patients for whom the initially decided surgery were MRM were able to undergo BCSpostNAC.<sup>7</sup>

**Aim of work:** is to compare response to neoadjuvant chemotherapy in locally advanced breast cancer with hormone receptor positive versus hormone receptor negative and its reflection on improving the surgical options in Egyptian patient population in Ain Shams University Hospitals.

## 2. Patients and Methods:

This is a prospective, observational study, conducted at Ain Shams University Hospitals. It started at March 2017 to December 2018. All patients who presented to our department were screened to select the candidates for our study.

The nature, scope, and possible consequences of the clinical study have been explained in a form that is understandable to the patients and they were consented to participate in the study.

The inclusion criteria to our study were; female patients known to have locally advanced breast cancer (T3 or T4 and/or N2), their age ranged from 20 to 80 years old, all patients were candidates for chemotherapy and all patients were initially candidates for MRM.

Currently there is no standard definition of LABC. However, it is usually characterized by one or more of the following features in absence of distant metastasis:

- The mass size is larger than 5 cm (T3).
- Tumor mass is adherent and fixed to: the skin or the chest wall (T4).
- Amalgamated ipsilateral axillary nodes (N2).<sup>8</sup>

Exclusion criteria were presence of one or more of the following criteria: distant metastasis, patients with inflammatory breast cancer (IBC), multicentric tumors, presence of second primary cancer, intolerance to chemotherapy due to associated serious co-morbidity or severe side effects.

All patients underwent a complete history taking, clinical and imaging examinations (e.g., bilateral sonomammography or MRI), to localize the mass and to estimate its primary size and the status of axillary LNs.

Tru-cut biopsy and immunohistochemistry (IHC) was done to all patients to diagnose and assess the pathologic features of the tumor. For the aim of ruling out distant metastasis the metastatic work up was done

in the form of CT scan (chest, abdomen and pelvis) and bone scan.

According to hormone receptor expression test results, patients were classified into two groups; Group A, hormone receptor positive, Group B, hormone receptor negative.

All patients received 4-8 chemotherapy cycles of a regimen which was decided by medical oncology staff doctors, according to one of the following protocols:

- FEC (fluorouracil, epirubicin, cyclophosphamide) + Docetaxel
- FEC (fluorouracil, epirubicin, cyclophosphamide) + Paclitaxel
- AC (doxorubicin, cyclophosphamide) + Docetaxel
- AC

**Primary endpoint:** The clinical response.

**Secondary endpoints:** pCR, BCS rate.

All patients were clinically examined before receiving each cycle of their treatment. Ultra sound imaging was done every two cycles of treatment. Ultra sound guided metal clipping of the mass was done to some cases which showed a great regression in the size of the mass.

According to the response to neoadjuvant therapy based on the RECIST criteria patients were divided into: Complete response CR group (the clinical and the radiological disappearance of the tumor within the breast and axillary lymph nodes), Partial response PR group (more than 30% reduction in the greatest tumor diameter), Stable disease SD group (neither response nor progression), progressive disease PD group (Tumors that increased more than 20% in the greatest diameter or the appearance of new disease)<sup>9</sup>.

After the completion of the neoadjuvant therapy course, patients were sent to surgery department and they underwent either MRM or CBS, with or without immediate reconstruction.

## Statistical analysis:

All results were tabulated and after data were checked for normality. The data were presented using numbers and percentage, wilcoxon test was used for comparison significance is considered at p value < 0.05. Data analysis was performed using the statistical package for social science, version 17 (SPSS Software, SPSS Inc., Chicago)

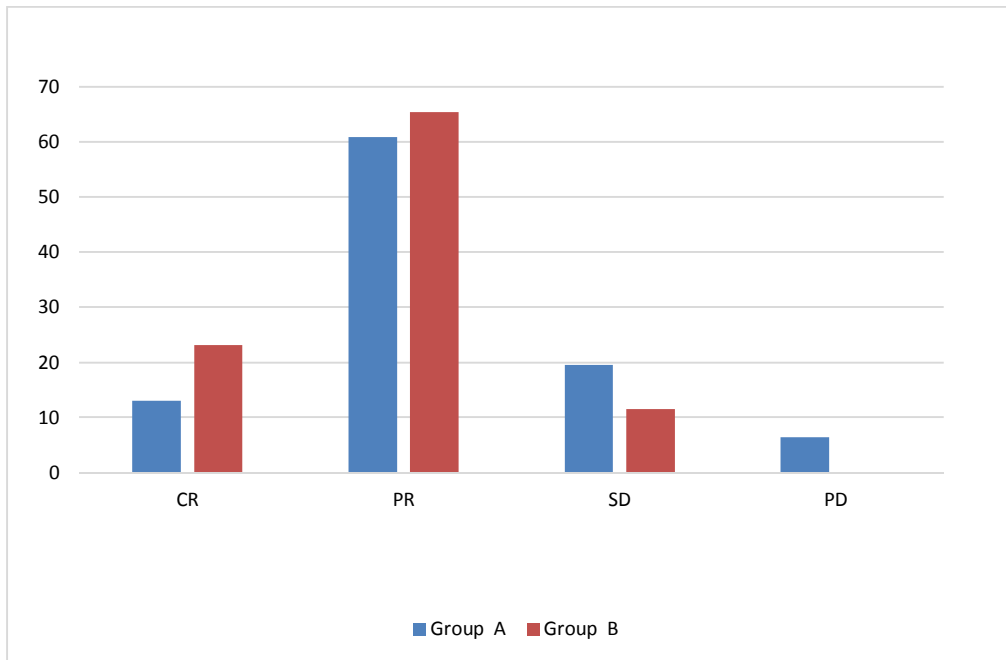
## 3. Results:

Prospective observational study originally included 72 patients.

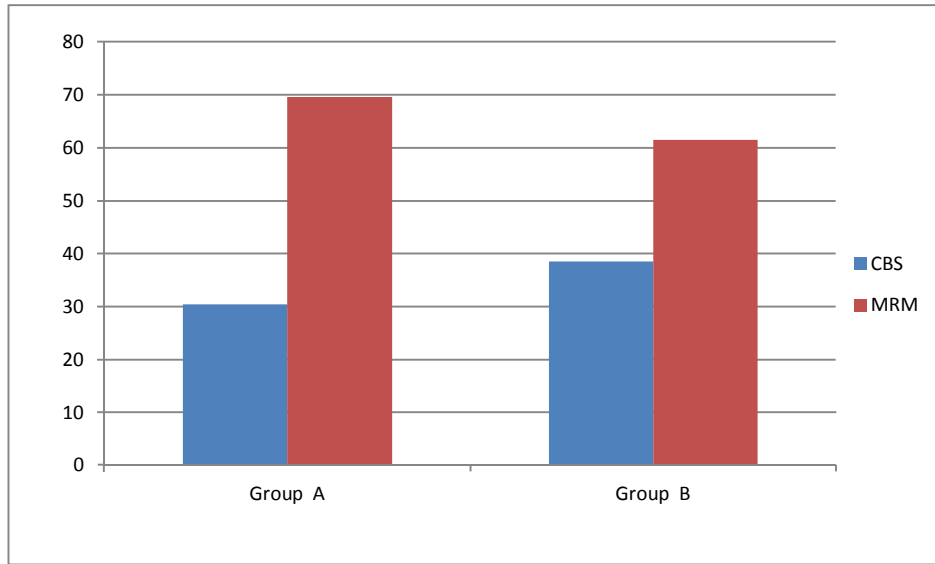
**Table 1. Illustrates patient's characteristics:**

	Group A HR +ve (46)		Group B HR -ve (26)	
Age	39-73		31-61	
Age of menarche	10-15		10-19	
Menopausal Status	Premenopausal	25 54.3%	15	57.7%
	Postmenopausal	21 45.7%	11	42.3%
Family history	9	19.6%	3	11.5%
Tumor size	5.1±1.6 cm (P value= 0.0001)		5.7±2.5 cm (P value= 0.0017)	
TNM classification:				
T <sub>3</sub>	35	76.1%	26	100
T <sub>4</sub>	11	23.9%	0	0%
Nodal status:				
+ve	39	84.8%	18	69.2%
-ve	7	15.2 %	8	30.7%
Histological type:				
IDC	46	100%	26	100%
Nuclear Grade				
G II	32	69.5%	12	46.2%
GIII	14	30.4%	14	53.8%
Her2 receptor status	27	58.7%	8	30.8%

Among the studied population the response to NAC is illustrated in (fig. 1). Both groups had a significant response (tumour size) to NAC (P value=0.0001).



**Figure 1:** Shows the response to NAC: Group A; represents HR +ve breast cancer patients. Group B; represents HR -ve breast cancer patients.



**Figure 2: Shows the reflection of NAC on the surgical option.**

Among over all 72 patients received NAC; CR was achieved in 12 patients (16.7%), their age ranged from 31-68ys, and 42.86% were postmenopausal. CR was achieved in 23% from total HR –ve and 13% of HR +ve.

**Table 2: illustrates the response to NAC:**

Response	Group A	Group B
CR	13.1%	23.1%
PR	60.8%	65.4%
SD	19.6%	11.5%
PD	6.5%	0%

All patients (72) underwent surgery (either MRM/CBS). In group A (46 patients), 32 patients underwent MRM (69.57%), 14 patients underwent CBS (30.43%) and pCR was achieved in 4 patients (8.6%). While, in group B (26 patients), 16 patients underwent MRM (61.54%), 10 patients underwent CBS (38.46%) and pCR was achieved in 5 patients (19.2%).

**4. Discussion:**

Historically, most patients who are diagnosed with LABC and considered operable were initially treated with radical mastectomy, and the results were disappointing; with 50% local recurrences (LR). The introduction of postmastectomy radiotherapy has improved the local control by 35%-55% and the survival by 25%-45%. However, by the addition of Adjuvant chemotherapy, hormonal therapy or both; the local control (LC) and overall survival (OS) have further more improved.<sup>10</sup>

Recently, NAC has been a main line of treatment for locally advanced breast cancer as it targets distant micrometastases.<sup>7</sup> It downstages the primary tumor and may convert the inoperable cases to operable and give a chance to a better surgical options,<sup>12</sup> in addition it provides information about the efficacy of chemotherapy.

NAC is tailored individually to each case based on the immunohistochemistry testing on tumor tissue that is collected by a core needle biopsy (Er, PR, HER2 receptors)<sup>13</sup>

Hormone receptors and HER-2 overexpression, are considered as a prognostic and predictive factors. A prognostic factor as it usually correlates with the natural history of the disease; disease-free survival or overall survival in the absence of systemic adjuvant therapy. Predictive factor; that predicts the response to a given therapy<sup>6</sup>.

The pathological complete response (pCR) post NAC has been a surrogate marker for the survival. Different trials with various chemotherapy regimens have shown pCR rates between 3 and 33 %<sup>11</sup>, which is matched with this study results; 16.7%.

Baseline characteristics were matched in this study groups to other trials' patients characteristics.<sup>11, 14, 15, 22</sup>

The majority of the patients (66.66%) whom had CR were postmenopausal which is matched with other studies.<sup>11, 14, 15, 16</sup>

The histological type in this study was IDC in 100% of patients which is matched with few studies<sup>11</sup>. And contrary to many other studies, The prevalent

pathological grade in our study was grade II (61%) which is similar to others.<sup>16, 17, 18</sup>

The percentage of HR+ve was 63.8% in our study and other studies.<sup>15, 16, 18</sup>

But Her2 receptor +ve patients in this study were 48.6% and other studies.<sup>11, 19</sup> while Her 2 +ve patients represented (20-25%) in most other studies. the change in the guidelines of assessment of Her 2 receptor over expression can explain the percentile difference (ASCO and the CAP Release Updated Guideline on HER2 Testing in Breast Cancer. [cited 2015 Feb 18]. <http://www.asco.org/presscenter/asco-and-cap-release-updated-guideline-her2-testingbreast-cancer>)

most of patients underwent MRM (66.67%) as few studies<sup>10, 11, 20</sup>, on the contrary of other studies in which BCS ranged 28-68%.<sup>14, 15, 16, 17, 21</sup>

## 5. Conclusions:

In patients with LABC; hormone receptor negative breast cancer have a better response to neoadjuvant chemotherapy and more liable to achieve pCR than hormone receptor positive breast cancer.

Primary treatment with neoadjuvant chemotherapy for LABC; can improve the surgical outcome and gives a chance for breast conservation rather than radical mastectomy without jeopardizing the oncological safety.

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