Zagazig University Medical Journal
www.zumj.journals.ekb.eg

July.2021 Volume 27 Issue 4
Manuscript ID ZUMJ-1910-1574
DOI 10.21608/zumj.2019.17825.1574

ORIGINAL ARTICLE

Outcome of the Locally Advanced Breast Cancer Patients in Zagazig University Hospital (Experience of Zagazig University Hospital)

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Submit Date 2019-10-09
Revise Date 2019-12-07
Accept Date 2019-12-20

ABSTRACT

Background: Worldwide, breast cancer is the most prevalence cancer in women. The prevalence of breast cancer about 29% of new cases of cancer and about 14% of cancer deaths in women, secondly to lung cancer as a cause of cancer-death, **Aim and objectives**: The aim of the current study was to study the outcomes of treatment of locally advanced breast cancer in Clinical Oncology and Nuclear Medicine Department in Zagazig University Hospitals. **Subjects and methods**: This retrospective cohort study was carried in Clinical Oncology and Nuclear Medicine Department in Zagazig University Hospitals, the included All old locally advanced breast cancer patients files in Clinical Oncology and Nuclear Medicine Department medical records of (2012 - 2013). **Results:** There was a significant statistical difference between group with distant metastasis and group with no distant metastasis regarding N system and stage of the tumor while there was no significant statistical difference regarding other parameters and there was no significant statistical difference between group with distant metastasis and group with no distant metastasis regarding radiotherapy. **Conclusion**: LABC in Egypt showed poor prognostic outcome and advanced management of locally advanced breast cancer required for improving chemotherapy regimens, predictors of chemotherapy response and imaging techniques

Keywords: LABC, Cancer, Retrospective, Oncology.

INTRODUCTION

In the United States of America (USA) every year there are about 180000 women were diagnosed with breast cancer. If increase of current rates still constant, a woman born today has a 1 in 10 percent for the development breast cancer [(1)].

Nearly 10–20% of the 13,000 diagnosed as breast cancer in Australia every year were locally advanced breast cancer [(2)]

In Egypt, the most prevalence cancer in women is the breast cancer, which represent about 18.9% of cancer cases (35.1% in women, 2.2% in men) according to the National Cancer Institute (NCI) series of 10 556 patients during the year 2001, with an age-adjusted rate of 49.6 per 100 000 population [(3)].

Breast cancer was classified into two groups depending on therapeutic management: early and locally advanced. Locally advanced breast cancer considered advanced breast cancer group. Clinical character of Locally advanced breast cancer was the tumor size > 5

cm (T3), with skin and chest wall involvement (T4), or inflammatory carcinoma and/or wide clinical lymph node (LN) involvement, and defined by the N2 and N3 categories according to the American Joint Committee on Cancer (TNM classification system) [4].

The prognosis of women with locally advanced breast tumors was heterogeneous and depending on size of tumor and the extent of lymph node involvement, and the presence or absence of inflammatory carcinoma. Women with locally advanced disease need multimodality therapy, and coordinated treatment planning between the clinical oncologists, surgical oncologist, is needed to optimize patient's care [5].

Dual HER2-targeted therapy combined with neoadjuvant chemotherapy had advanced improvement in the rates of pathological complete response with good toxicity profile and must be considered as an integral part of treatment along with surgery and radiation therapy. Nonetheless, despite advances in the understand of genomic nuances of breast cancer, targeted therapies still an unmet need for the treatment of locally advanced breast cancer from HER2-positive tumors [1].

AIM OF THE STUDY

The aim of this work was to study the outcomes of treatment of locally advanced breast cancer in Clinical Oncology and Nuclear Medicine Department in Zagazig University Hospitals

PATIENTS AND METHODS

This retrospective study was carried in Clinical Oncology and Nuclear Medicine Department, Zagazig University hospital and included patients all old locally advanced breast cancer patients files (150 cases) in Clinical Oncology and Nuclear Medicine Department medical records of (2012 - 2013) will be included in the study.

The main information for locally advanced breast cancer registration includes personal data identification, demographic data, date and most valid basis for diagnosis, pathology and hormonal profile of the tumor and details of treatment.

Written informed consent was obtained from all children' parents, the study was approved by the research ethical committee of Faculty of Medicine, Zagazig University. The study was done according to The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Inclusion criteria:

All old locally advanced breast cancer patients files in Clinical Oncology and Nuclear Medicine Department, Zagazig University hospital medical records (2012 and 2013).

Exclusion criteria:

No file was excluded.

All patients files were subjected to the following:

Personal Data, demographic characteristics, Date and most valid basis of diagnosis, Pathology of the tumor, Hormonal profile of the tumor and Treatment details.

Statistical analysis

Data were collected, tabulated and analyzed by SPSS 20, software for Windows. The significance level considered at $P < 0.05$.

RESULTS

Table (1), showed the demographic data of our patients showing that mean age was 48.5 ± 10.9, about half of patients were post-menopausal , 38.7% of them were pre-menopausal and only 10% of the patients had positive family history. Table (2), showed that the majority of the patients had been diagnosed by excisional biopsy 85.3% , MRM was commonest surgery performed 85.3%, 73.3 %of the patients had IDC as pathological subtype, LVI was shown in 40.7% of the patients, while ECI shown in 32% of the cases. Table (3), showed that 34.6% of patients presented with pathological T3 and 38.7% with T4, 52.6% with pathological N3, 51.4% of them were stage IIIC. The number of patients with ER +ve was 75.3%, PR +ve was 71.3% while (42%) had +ve her2/neu receptors. Table (4), showed that the most of patients were on AC+ Taxol chemotherapy with the mean chemotherapy duration was 3.4 ± 0.5, five Patients refused to take chemotherapy, the commonset neoadjuvant was CAF with PCR represented 12 patient

(8.27%). Table (5), showed that 128 patients (82%) received post mastectomy radiotherapy with the with chest wall and lymphatics 50Gy/25fx/5 weeks and only 22(14.7%) patients received whole breast irradiation in hypofractionated schedule 40Gy-15fx/3 weeks followed by boost to tumor bed 10-16Gy 3/5fx/1-1.5 week, 5-8Fx/1-1.5 week. Table (6), showed that Herceptin was indicated in 40% of patients, 48.0% AI alone and 42.0% were on Tamoxifen alone and 33.3% received Herceptin and hormonal therapy less than 5 years, 3 patient didn't take Herceptin due to cardiac co-morbidity . Table (7), showed that 52% of patient had distant metastasis, 17.3% had local recurrence and 10.7% had locoregional recurrence while 20% had no relapse. The commonest site of metastasis was the bone in 33.3% of patients. Table (8), showed that local recurrence has significantly difference with tumor size as well as tumor stage. Table (9), showed that there was a statistical significant difference between group with locoregional recurrence and group with no locoregional recurrence regarding T system and staging while there was no significant statistical difference regarding other parameters. Table (10), showed that there was a statistical significant difference between group with distant metastasis and group with no distant metastasis regarding N system and stage of the tumor while there was no significant statistical difference regarding other parameters.

Table (1): demographic data of the whole study population

Demographic data	All patients
Count (%)	150 (100%)
Age (years)	
Mean ± SD	48.5 ± 10.9
Median (IQR)	49 (40 – 56.5)
Menstruation	
Peri-menopause	15 (10.0%)
Pre-menopausal	58 (38.7%)
Post-menopausal	77 (51.3%)
Marital status	
Single	10 (6.7%)
Married	112 (74.7%)
Divorced	28 (18.6%)
Parity	
Nullipara	43 (28.7%)
Multipara	107 (71.3%)
Others	
Oral contraceptives	55 (36.7%)
Breast feeding	83 (55.3%)
Family history	15 (10.0%)

Table (2): tumor characteristics of the whole study population

Tumor characteristics	All patients
Count (%)	150 (100%)
Biopsy type	
FNAB	9 (6.0%)
Core biopsy	13 (8.7%)
Excisional	128 (85.3%)
Surgery type	
MRM	128 (85.3%)
BCS	22 (14.7%)
Laterality	
Right	58 (38.6%)
Left	76 (50.7%)
Bilateral	16 (10.7%)
Pathology	
IDC NOS	110 (73.3%)
ILC	36 (24.0%)
Paget's	4 (2.7%)
Post-excision margin	
Positive	60 (40.0%)
Grade	
Grade I	3 (2%)
Grade II	116 (77.3%)
Grade III	31 (20.7%)
Others	
LVI	61 (40.7%)
ECI	48 (32%)

Table (3): tumor staging of the whole study population

Tumor staging	All patients
Count (%)	150 (100%)
N. of positive LNs	
Mean ± SD	12.9 ± 8.2
Median (IQR)	12 (2 – 20)
Tumor size (cm)	**N=77, missing=73**
Mean ± SD	4.7 ± 3.1
Median (IQR)	4 (3 – 6)
T system	
T1	0 (0.0%)
T2	40 (26.7%)
T3	52 (34.6%)
T4	58 (38.7%)
N system	
N0	0 (0.0%)
N1	12 (8%)
N2	59 (39.4%)
N3	79 (52.6%)
Stage	
Stage IIIA	44 (29.3%)
Stage IIIB	29 (19.3%)
Stage IIIC	77 (51.4%)
Receptors	
ER	113 (75.3%)
PR	107 (71.3%)
HER2/neu +VE	63 (42%)

Table (4): Chemotherapy of the whole study population.

Chemotherapy	All patients
Count (%)	150 (100%)
Chemotherapy regimen	
FEC	15 (10%)
FEC+Taxol	10 (6.7%)
FEC+3Taxotere	3 (2%)
AC+Taxol	87 (58%)
CAF	28 (18.7%)
CMF	2 (1.3%)
Chemotherapy duration	
Adjuvant 21 days	128 (85.33%)
Neo Adjuvant 21 days *4	22 (14.7%)
Chemotherapy duration	
Mean ± SD	3.4 ± 0.5
Median (IQR)	3 (3 – 5)

Table (5): radiotherapy of the whole study population.

Radiotherapy	All patients
Count (%)	150 (100%)
Target volume	
Whole breast	22 (14.7%)
Chest wall + lymphatics	128 (82%)
Radiation dose	
40Gy/15fx/3 weeks+10_16Gy 5-8fx (boost)	22 (14.7%)
50Gy/25fx/ 5 weeks	128 (82%)
Machine	
Cobalt	41 (27.3%)
Linac	109 (72.7%)
2D	60 (40.0%)
3D	90 (60.0%)
Boost	
Yes	22 (14.7%)

Table (6): Herceptin and Hormonal therapy of the whole study population.

Herceptin and hormonal therapy	All patients
Count (%)	150 (100%)
Herceptin	
Indicated	60 (40%)
Schedule	
Weekly	4 (6.7.1%)
21 days	56 (93.3%)
Duration	
<12 months	23 (36.5%)
12 months	40 (63.5%)
Hormonal regimen	
Tamoxifen Alone	63 (42.0%)
Al Alone	72 (48.0%)
Tam then Al	15 (10.0%)
Treatment duration	
< 5 years	50 (33.3%)
5 years	100 (66.7%)

DISCUSSION

Breast cancer considered the most invasive cancer in women and causes cancer death in women after lung cancer. Screening the symptoms very important to reduce the risk. [6].

The incidence of LABC in Egypt represented 33.24% according to the Gharbiah Population Based Registry [7].

Locally advanced breast cancer is characterized by the most advanced breast tumours with absence of distant metastasis. The need to identify LABC as a separate group of breast cancers arose in view of the

high associated rate of locoregional & systemic failure (in the absence of distant metastasis at presentation) although the surgeons efforts for removing the locoregional spread of the tumour in its entirety. It was recognized that multimodality treatment (surgery, chemotherapy, and radiotherapy in combination with hormonal and targeted therapy if required) can significantly improve outcomes in this select group of patients [8].

The current study showed that the mean age was 48.5 ± 10.9, about half of patients were post-menopausal , 38.7% of them were pre-menopausal and only 10% of the patients had positive family history while in **Mona et al.** [1] the mean age was 53.46±11.22 and in study of **Agodirin et al** [9] was 47.7±11.7.

In the present study the majority of the patients had been diagnosed by excisional biopsy 85.3% , MRM was commonest surgery performed 85.3%,73.3 %of the patients had IDC as pathological subtype, LVI was shown in 40.7% of the patients, while ECI shown in 32% of the cases. 34.6% of patients presented with pathological T3 and 38.7% with T4, 52.6% with pathological N1 8% pathological N2 39.4%,pathological N3, 51.4% of them were stage IIIC. The number of patients with ER +ve was 75.3%, PR +ve was 71.3% while (40%) had +ve her2/neu receptors.

Our results are supported by findings reported by **Mona et al.** [1] as they reported that ER and PR+ was observed in 60 and 56%, respectively, which showed comparable results to studies conducted by **Bonnefoi et al.** [10] which done on LABC, with 32 and 66%, respectively. However, Her2/neu+ was detected in 13%, which is less than that reported in other study done on LABC (26 and 55%) conducted by **Akhsan and Aryandono** [11] .

Our results show that Herceptin was indicated in 40% of patients, where 3 patient didn't receive it due to cardiac co-morbidity ,48.0% AI alone and 42.0% were on Tamoxifen alone and 33.3% received hormonal therapy less than 5 years.

In the present study, the period of median follow up was 46 months 52% of patient had distant metastasis, 17.3% had local recurrence and 10.7% had locoregional recurrence while 20% had no relapse. The commonest site of metastasis was the bone in 37.3% of patients.

The current study was in agreement with the results of **Koca et al.** [12] as they reported that after 39.5 months of median follow-up, 96 patients (44%) had relapse and 64 (30%) were patients died.

In the current study 52% of patient had distant metastasis, 17.3% had local recurrence and 10.7% had locoregional recurrence while 20% had no relapse. The commonest site of metastasis was the bone in 37.3% of patients.

In the present study there was no significant difference between group with local recurrence and group with no local recurrence regarding demographic data and tumor characteristics.local recurrence shown significantly difference with tumor size as well as tumor stage.There was no significant difference regarding chemotherapy regimen and duration , radiotherapy nor Herceptin and hormonal therapy.

Our results showed that there was no statistical significant difference between locoregional recurrence and demographic data, tumor characteristics, chemotherapy, radiotherapy, Herceptin and hormonal therapy. There was statistical significant difference between group with locoregional recurrence and group with no locoregional recurrence regarding T system and staging. which are supported by findings reported by **Klein et al.** [13] where they showed that the cohort was distributed between patients with stage II (51%) and stage III (49%) disease. There was no significant difference between the studied groups regarding LRR. There statistical significant RFS difference (p = 0.04), with 5-year RFS for stage II 83% and 58% in stage III patients. 5-year OS rate was 86% in stage II patients and 72% in stage III patients with no statistical significant difference (p = 0.46).

In the present study there was no significant difference between distant metastasis and demographic data, tumor characteristics,

chemotherapy regimen, radiotherapy, Herceptin and hormonal therapy. There was significant difference between group with distant metastasis and group with no distant metastasis regarding N system and stage of the tumor and chemotherapy.

Klein et al. [13] reported that distant recurrence alone in 15 patients was twice to LRR alone (7 patients), which agree with the results of **White et al.**[14] after NAC and surgery. Molecular subtype did not significantly affect recurrence or survival rates.

Conclusion: LABC in Egypt showed poor prognostic outcome and advanced management of locally advanced breast cancer required for improving chemotherapy regimens, predictors of chemotherapy response and imaging techniques

No Conflict of Interest
No financial disclosure

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How to Cite

Abdel hakiem, N., El-Sawy, W., Ahmed Almoghraby, S., Elsayed, R. Outcome of the Locally Advanced Breast Cancer Patients in Zagazig University Hospital (Experience of Zagazig University Hospital). Zagazig University Medical Journal, 2021; (759-766): -. doi: 10.21608/zumj.2019.17825.1574