

Clinicopathological Characteristics and Survival of Triple-Negative Breast Cancer Patients: A Single Institution Study from Egypt

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Background: Triple-negative breast cancer (TNBC) is a subtype of breast cancer that is characterized by being more aggressive, presentation in younger age, and higher response rate to chemotherapy. It is more likely to recur and to metastasize early.

Methods: Retrospective review of the medical records of TNBC patients treated in a single Egyptian cancer center during a 4-year period.

Results: Sixty-five patients were included. Forty-six percent of patients were < 50 years old and 22% had a positive family history. Ten (15%) patients were metastatic at presentation. Modified radical mastectomy was performed in 42% of patients and adjuvant chemotherapy was administered in 55% of them. Relapse occurred in 12 (22%) out of 55 patients who had no distant metastasis at presentation (M0). The overall survival rate of M0 patients at 12, 24 and 36 months was 96%, 91% and 88%; respectively. The disease-free survival rate of M0 patients at 12, 24 and 36 months was 90%, 81% and 71%; respectively.

Conclusion: TNBC is an aggressive subtype of breast cancer that occurs at younger age. Frequently, it is of high grade and presents in an advanced stage.

Keywords: Triple-negative breast cancer, Clinicopathological characteristics, Treatment outcome, Egypt

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INTRODUCTION

Triple-negative breast cancer (TNBC) is a subtype of breast cancer that tests negative for estrogen receptors (ER), progesterone receptors (PR) and Her2 protein which means that the proliferation of this type of cancer is not fueled by the estrogen and progesterone hormones or by the Her2 protein¹. That is why TNBC does not respond to hormonal therapy or to drugs that target Her2 protein receptors².

Triple-negative breast cancer constitutes about 10-20% of breast cancers^{3,4}. It is more aggressive and has a poorer prognosis than other types of breast cancer as studies have shown that TNBC is likely to metastasize early at presentation and to recur after treatment⁵. It tends to present with a higher grade than other subtypes and usually has a basal-like cellular morphology¹.

Patients with TNBC are more likely to be < 50 years of age and about 70% of them have an inherited BRCA mutation, particularly BRCA1 mutation⁶.

This study describes the clinicopathological characteristics, management, recurrence rate and survival of TNBC patients treated in a single cancer institution in Egypt.

METHODS

This retrospective study included TNBC patients treated at the Kasr Al-Ainy Center of Clinical Oncology

and Nuclear Medicine – Cairo University Hospitals in the period from 2011 to 2014.

After obtaining the institutional ethical approval, the medical records of breast cancer patients were reviewed.

Adult (> 18 years of age) females with immunohistochemistry (IHC) negative expression of ER, PR and Her2Neu were included in the study. Those who had Her2Neu +1 or +2 expression by IHC were included after being proved to be negative by Fluorescence in-situ hybridization (FISH) result.

A total of 162 TNBC patients were identified. Only 65 (40.1%) of them were included in the study. The remaining patients were excluded because of loss of records, incomplete documentation or loss to follow up.

The data retrieved included: patients' characteristics (age at diagnosis, menopausal status and family history), tumor characteristics (grade, size, nodal involvement and metastases at presentation), treatment received (surgery, chemotherapy and radiotherapy) and recurrence data (type, site and date) if any.

Data were described in terms of mean \pm standard deviation (SD) or frequencies and percentage when appropriate. The mean and median disease-free survival (DFS) and overall survival (OS) were estimated using the Kaplan-Meier method. P value < 0.05 was considered statistically significant. Statistical analyses were done using IBM SPSS (Statistical Package for the Social Science) software for Microsoft Windows, release 22 (IBM corp., Armonk, NY, USA).

RESULTS

Triple-negative breast cancer represented 10% of all breast cancer treated at our institution during the study period.

Personal characteristics of the included 65 patients are shown in table 1. The mean age of patients at diagnosis was 49.2 years (± 13.1) and almost half of them were below 50 years old. Positive family history was present in 21.5% of the patients; all were breast cancer except one patient who gave family history of endometrial carcinoma.

Table 1: Patients' characteristics (n= 65)

Variable	No.	%
Age at diagnosis		
< 50 years	30	46.2
≥ 50 years	35	53.8
Family History		
Negative	51	78.5
Positive	14	21.5
Menopausal status		
Premenopausal	32	49.2
Postmenopausal	33	50.8

Table 2 illustrates tumor characteristics and treatment lines received. The most common histopathological type was infiltrating duct carcinoma and approximately one third of patients had grade III tumor. At presentation, almost half the patients had positive lymph nodes and 15% had distant metastases.

The percentage of patients who underwent modified radical mastectomy (MRM) or breast conservative surgery (BCS) was 79%. Adjuvant chemotherapy was administered in 55.4% of the patients while neoadjuvant chemotherapy was administered in 44.6% of patients. An anthracycline-based chemotherapy regimen was the most commonly regimen used, being administered in 61.5% of patients. Adjuvant radiotherapy was given to 71% of patients.

Relapse occurred in 12 (21.8%) patients out of the 55 who were not metastatic at diagnosis. Bone was the most common site of distant metastasis followed by lung then liver. Only one patient developed brain deposits.

The OS rate of non-metastatic (M0) patients was 96% at 12 months, 91% at 24 months and 88% at 36 months. Their mean OS time was 57.7 months (95% Confidence Interval [CI]: 53.7 – 61.6) and the median OS was not reached. The 5-year OS rate was 88% (figure 1).

The mean OS of metastatic (M1) patients was 23.2 months (95% CI: 15.75 – 60.69) and the median OS was 28.4 months (figure 1).

The DFS rate of M0 patients at 12, 24 and 36 months was 90%, 81% and 71%, respectively. The 5-year DFS rate was 71% (figure 2).

The 12-months OS rate of patients who received neoadjuvant chemotherapy was 84% while it was 97% for those who received adjuvant chemotherapy ($p = 0.054$) (figure 3).

Table 2: Tumor characteristics and treatment (n= 65 patients)

	No.	%
Histopathology		
Infiltrating duct carcinoma	61	93.8
Medullary carcinoma	2	3
Intraductal carcinoma	1	1.5
Mixed	1	1.5
Grade		
II	41	63.1
III	19	29.2
Unknown	5	7.7
T-stage		
T0	5	7.7
Tis	1	1.5
T1	5	7.7
T2	28	43.1
T3	10	15.4
T4	4	6.2
Unknown	12	18.5
N-stage		
N0	22	33.8
N1	11	16.9
N2	13	20
N3	7	10.8
Unknown	12	18.5
Distant metastases at diagnosis		
M0	55	84.6
M1	10	15.4
Surgery		
Biopsy	13	20
Modified radical mastectomy	27	41.5
Breast conservative surgery	24	37
Partial mastectomy	1	1.5
Chemotherapy aim		
Neoadjuvant	29	44.6
Adjuvant	36	55.4
Chemotherapy regimen		
Doxorubicin – cyclophosphamide (AC) / Paclitaxel	40	61.5
Others	25	38.5
Radiotherapy		
Adjuvant	46	70.7
Palliative	12	18.5
Not given	7	10.8

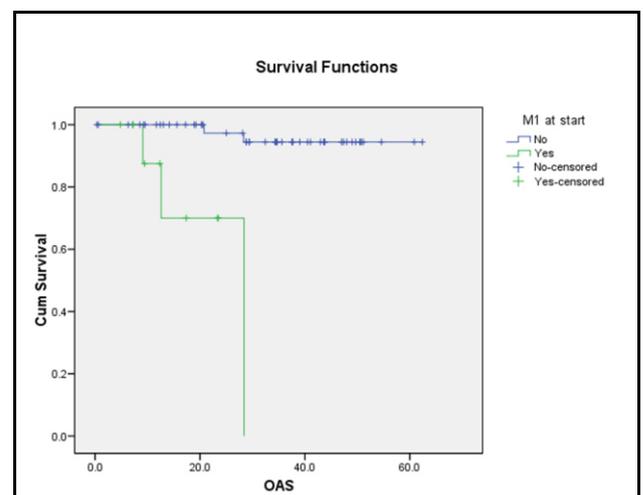


Figure 1: Kaplan-Meier curves of estimated overall survival according to metastatic status at diagnosis

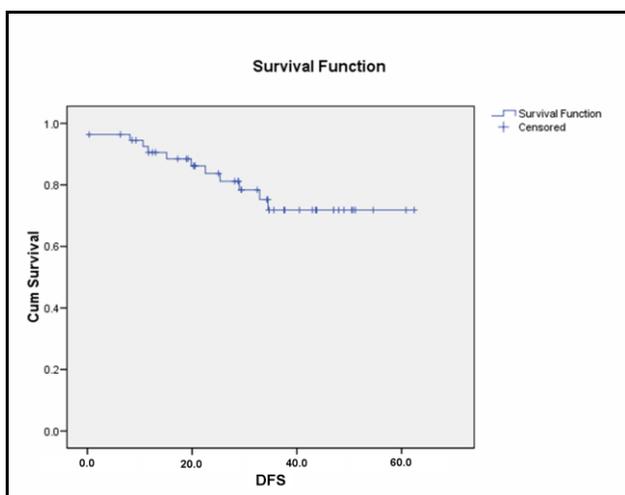


Figure 2: Kaplan-Meier curve of estimated disease-free survival of M0 patients

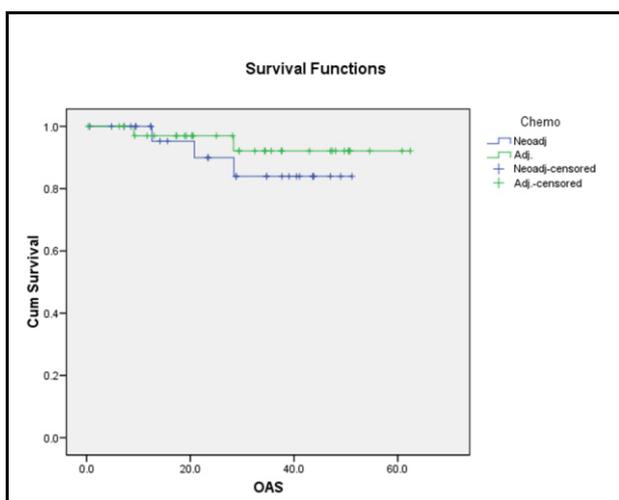


Figure 3: Kaplan-Meier curves of estimated overall survival of patients who received adjuvant vs. neoadjuvant chemotherapy

DISCUSSION

Triple-negative breast cancer is known by its aggressive clinicopathological features. It presents at a younger age with larger tumor size and higher grade and tends to metastasize and recur after treatment ⁷.

At our institution, representing a lower-income setting, TNBC represents 10% of all breast cancer cases, which is comparable to most of the studies which reported an incidence ranging from 10% to 20% ⁴.

The mean age of TNBC in our study was 49 years, which is similar to many other studies including those from Egypt where a recent study conducted at the Egyptian National Cancer Institute found a similar mean age of 49 years ⁸. However, some other studies reported different mean age ranging from 44 to 56 years ^{5,7}.

Positive family history was documented in 22% of our patients similar to that reported by Fayaz et al from Kuwait ⁹, while Ghosn et al reported a family history in 10% of patients with TNBC in Lebanon ¹⁰.

Invasive duct carcinoma is the predominant histopathology type in our study being presented in 94%

of our patients similar to studies done in Singapore [11] and Japan ^{11,12}.

Most of the cases in our study were T2 stage (43%) followed by T3 (15%), and grade II (63%) followed by grade III (24%). This is compatible with the aggressive nature of TNBC which is usually of high grade and large tumor size as reported by other studies ¹³.

Zhang et al ¹⁴ and Dent et al ¹⁵ reported a percentage of node positivity among TNBC cases higher than that among our patients. This may be attributed to the small number of patients included in our study. However, Lin et al and other related studies reported that TNBC was less likely to be lymph node positive ¹⁶.

In our study the 1-year OS rate was 84% for patients who received neoadjuvant chemotherapy, which was lower than the 97% rate of those who received adjuvant chemotherapy. This could be attributed to the fact that neoadjuvant chemotherapy is administered to patients presenting with more advanced disease to downstage it. However, difference between the two groups was not statistically significant. It is difficult with the current study design and sample size to come out with a conclusion regarding that issue.

The 5-year OS rate in our study was 88% which is comparable to that reported by a study from China where the 5-year OS rate was 88.5% ¹⁷, and another study from Iran where the 5-year survival was 86.1% ¹⁸. On the other hand, the 5-year OS rates were much lower in other studies. A study from New Zealand reported a 5-year OS rate of 72% ¹⁹ and another study from Brazil done by Gonçalves et al reported a rate of 62% ²⁰. This was similar to the 64% rate found by Liedtke et al ²¹. The higher 5-year OS rate in our study could be attributed to the earlier stage (T2 and T3) at presentation among our patients. Studies that reported lower 5-year OS rates included patients with more advanced stage, mostly T3 and T4 at presentation.

Conclusion

Triple-negative breast cancer is an aggressive subtype of breast cancer that occurs among younger patients (< 50 years old) and usually presents with large tumor size and high grade. This confirms that the clinicopathological characteristics of TNBC among Egyptian female patients are more or less similar to that in other regions of the World. To improve the treatment outcome of TNBC, novel therapies are needed, such as the PARP inhibitors and antiandrogens. Patients should be encouraged to be treated in large clinical studies that are well-designed using the newly developed molecularly targeted therapy.

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