Original Article

# Analysis of Recurrence Time and Its Patterns in Triple Negative Breast Cancer

Recurrence of Triple Negative Breast Cancer

Sarah Khan, Ahmed Ijaz Masood and Zil-e-Huma


## ABSTRACT

**Objective:** To evaluate the pattern and time of recurrence of triple negative breast cancer among patients treated in a tertiary care hospital.

**Study Design:** Descriptive study

**Place and Duration of Study:** This study was conducted at the Department of Radiotherapy & Oncology, Nishtar Hospital Multan January 2014 to December 2018.

**Materials and Methods:** Forty females who presented with recurrence of triple negative breast cancer were included. Data of baseline variables at the time of first diagnosis, treatment required, and time of first recurrence was noted for each patient.

**Results:** There were 30 (75%) having age 35-60 years who presented with recurrence. Invasive ductal carcinoma was commonest in patients of recurrence with prevalence rate of 85%. Recurrence occurred within first 06 months in 08 (20%) patients and in 24 (60%) within 06 to 12 months. Regional recurrence occurred in 14 patients, out of which 08 (57.1%) were having axillary involvement. All of the 40 patients were having distant meta-stasis.

**Conclusion:** Recurrence is very common within first 12 months after primary treatment in patients with triple negative breast cancer. In present study, recurrence occurred in 80% patients after primary treatment. Loco-regional recurrence occurred in 65% patients, and all of the patients developed subsequent metastasis.


**Key Words:** Triple negative breast cancer, Recurrence, Pattern

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## INTRODUCTION

Breast cancer is the common cancer in female gender. Worldwide about 1.67 million cases of new breast cancer were diagnosed in 2012, which accounted for 25% of all cancers.[1] In Pakistan, the incidence of breast cancer is highest among Asian nations.[2] According to reports 1 in 9 females suffer from breast cancer at some stage of life.[3] Mortality from breast cancer has reduced remarkably in the last 3 decades, Like in Australia the mortality rate reduced from 50/100,000 females to 38/100,000 in 2000.[4] The reduction in mortality in patients of breast cancer is due to multiple factors such as availability of early screening tools and management in early stage and availability of modern treatment methods.[5]

Triple negative breast cancer (TNBC) first classified by Brenton et al in 2005, is a type of carcinoma in which there is absence of progesterone receptors (PR) and estrogen receptors (ER) and deficiency of over-expression of HER2 gene.[6] About 15% to 20% of all cases of breast cancer are diagnosed as TNBC.[7] TNBC has more aggressive clinical progression with highest risk of metastasis especially central nervous and visceral system. Prevalence is much higher in Afro-American females.[8]

Regarding treatment TNBC is chemo-sensitive but its optimal treatment is a major challenge, recurrence rate is much higher, in majority reoccurrence is diagnosed in only 3-5 years of primary treatment.[9,10] Average reoccurrence time is 19-40 months as compared to 35-67 months in non-TNBC patients.[11-13] Prognosis is also poor in these patients with reduced long-term life expectancy.[14]

## MATERIALS AND METHODS

This descriptive study was carried out at Department of Radiotherapy & Oncology, Nishtar Hospital Multan 1st January 2014 to 31st December 2018 and came back with recurrence till January 2019. We included in the data of 40 female patients who were treated for primary management of TNBC. Data of all patients was retrieved from the medical record room of the patients. Patient's of breast cancer other than TNBC was taken as exclusion criteria. Primary objectives of study were local recurrence (LR), regional recurrence (RR), site of sub-sequent meta-stasis and timing of recurrence. Local recurrence was labeled if recurrence involved chest wall. Regional recurrence was labeled if the tumor re-

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appeared in ipsilateral or contra-lateral axillary, cervical or supra-clavicular lymph nodes. Distant meta-stasis was labeled if tumor had spread to bones and visceral organs including liver, lungs, or brain. Data of baseline variables at the time of first diagnosis, treatment given, and time of first recurrence was noted for each patient. The data was entered and analyzed through SPSS-20.

# RESULTS

There were 30 (75%) patients having age 35-60 years who presented with recurrence, while remaining 25% were having age <35 years. Stage of TNBC at the time of initial diagnosis was II in 50% patients and III in 35% patients. Invasive ductal carcinoma was commonest in patients of recurrence with prevalence rate of 85%. During primary treatment, neoadjuvant chemotherapy was given to 24 (60%) patients and adjuvant chemotherapy was given to only 16 (40%) patients.

**Table No.1: Demographic information of the patients**

| Variable | No. | % |
|---|---|---|
| Age at the time of first diagnosis of TNBC | | |
| <35 Years | 10 | 25.0 |
| 35-60 Years | 30 | 75.0 |
| Stage at the time of diagnosis | | |
| Stage I | - | - |
| Stage II | 20 | 50.0 |
| Stage III | 14 | 35.0 |
| Stage IV | 6 | 15.0 |
| Histological diagnosis | | |
| Invasive ductal | 34 | 85.0 |
| Invasive Lobular | 2 | 5.0 |
| Poorly differentiated | 4 | 10.0 |
| Chemotherapy | | |
| Adjuvant | 16 | 40.0 |
| Neo-adjuvant | 24 | 60.0 |
| Drugs used for chemotherapy | | |
| Anthracyclines | 28 | 70.0 |
| Anthracyclines plus Taxanes | 12 | 30.0 |
| Surgery type | | |
| Mastectomy | 4 | 10.0 |
| Modified radical mastectomy | 32 | 80.0 |
| Lumpectomy | 4 | 10.0 |
| Treatment given after recurrence | | |
| Systemic Chemotherapy | 40 | 100.0 |
| Type of systemic chemotherapy | | |
| Cyclophosphamide methotrexate fluorouracil (CMF) | 8 | 20.0 |
| Gemcitabine and cisplatin | 18 | 45.0 |
| Capecitabine | 14 | 35.0 |
| Adjuvant radiation | 35 | 87.5 |
| Lines of chemotherapy after metastasis | | |
| 0 | - | - |
| 1 | 6 | 15.0 |
| 2 | 26 | 65.0 |
| 3 | 8 | 20.0 |

**Table No.2: Frequency of site of recurrence**

| Variable | No. | % |
|---|---|---|
| Loco-regional Recurrence | 26 | 65.0 |
| Local recurrence (Chest wall) | 12 | 30.0 |
| Regional recurrence | 14 | 35.0 |
| Supra-clavicle | 2 | 14.28 |
| Cervical | 4 | 28.5 |
| Axillary | 8 | 57.1 |
| **Site of subsequent meta-stasis** | | |
| Liver | 8 | 20.0 |
| Lung | 14 | 35.0 |
| Bone | 2 | 5.0 |
| Brain | 16 | 40.0 |

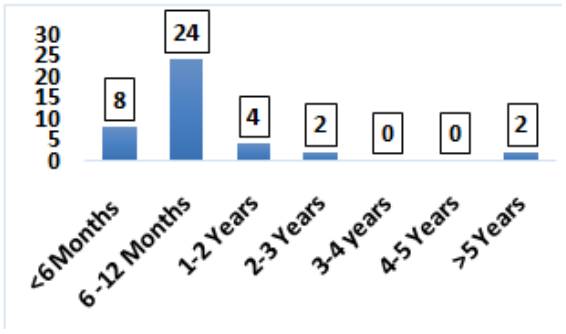


**Figure No. 1: Time of recurrence of TNBC**

After chemotherapy, modified radical mastectomy was done in 32 (80%) patients, simple mastectomy in 4 (10%) and lumpectomy in 4 (10%) patients. After recurrence, systemic chemotherapy was given to all patients. Gemcitabine and cisplatin chemotherapy was given to 18 (45%) patients, Cyclophosphamide Methotrexate Fluorouracil (CMF) to 8 (20%) while capecitabine chemotherapy was given to 14 (35%) patients (Table 1). Recurrence occurred within first 6 months in 8 (20%) patients and in 24 (60%) patients within 6 to 12 months (Fig. 1). Loco-regional recurrence occurred in 26 (65%) patients, while all of the 40 patients developed distant metastasis. In patients having regional recurrence, axillary involvement was found in 8 (57.1%) patients, cervical involvement in 4 (28.5%) and supraclavicular involvement in 2 (14.28%) patients (Table 2). After reoccurrence, contralateral breast was involved in 04 (10%) patients. Secondary malignancies developed in 3 patients, Ca ovary in 2 (5%) and colorectal cancer in 01 (2.5%) patients.

# DISCUSSION

In last 25 years, significant improvements have occurred in cancer treatment particularly due to development of hormone therapy. The second major achievement is development of specific HER2 receptor targeting treatments.[15] The 3rd evolution is the recognition of hormone receptor status such as PR and ER receptors. This recognition gave rise to the

identification of TNBC.[8] Triple negative breast cancer is more chemo-sensitive as compared to the other cancers. Therefore, chemotherapy is still the mainstay treatment for TNBC.[16]

In present study, we reported the clinical pattern of recurrence of TNBC. Out of 40 patients who presented to us with recurrence, 26 (65%) patients were with loco-regional recurrence (12 (30%) with local recurrence and 14 (35%) with regional recurrence) while metastasis was found in all patients.

A study done by Steward et al[17], on follow-up of 414 patients of TNBC patients reported recurrence in 110 patients in a mean follow-up period of 68 months. Out of these 110 patients there were 19 (17.27%) patients who presented with loco-regional meta-stasis, 70 (63.63 %) with distant meta-stasis and 21 (19.09%) with loco-regional plus distant meta-stasis. In their study, the patients who presented with recurrence, neo-adjuvant therapy was given to only 36.4% patients. Regarding surgical treatment, partial mastectomy was done in 57.5% patients, simple mastectomy in 14% and redical mastectomy in 28.5% patients. While in our study, neo-adjuvant chemotherapy was given to 60% patients.[18] Regarding surgical management, simple mastectomy was done in 10% patients, modified radical mastectomy in 80% patients, and lumpectomy in 10% patients.

A study conducted by Khanna et al[8] reported recurrence in 26 patients, out of these 17 (60.71%) presented with loco-regional recurrence and 11 (39.3%) patients were having distant meta-stasis. The most common site of meta-stasis was visceral, there was no patient who had bone meta-stasis.[8] Another study by Radosa et al[19] local recurrence occurred in 17 (6%) patients, chest wall recurrence in 24% patients and breast recurrence in 76% patients. Regional recurrence occurred in 5 (2.0%) patients, out of which axilla was involved in 3 (60%) patients and intra-memory lymph nodes (LN) in 2 (40%) patients. In patients with distant meta-stasis, brain involvement was found in 16% cases, bones in 14%, and multiple sites in 36% patients. In our study, regional recurrence occurred in 14 patients, out of which 08 (57.1%) were having axillary involvement, 04 (28.5%) cervical and 02 (14.28%) supra-clavicular involvement. While our all patients were having distant metastasis, 8 (20%) patients were having liver involvement, 14 (35%) lung, 2 (5.0%) bone and 16 (40%) brain meta-stasis.

In present study, 08 (20%) patients presented with recurrence within first 06 months, 24 (60%) within 1 year, there were only 2 (5.0%) patients who presented after 5 years of follow-up. Steward et al. reported that 80% of patients of TNBC after primary treatment present with recurrence within 3 years. A study by Gonçalves et al[20] on disease free survival of TNBC and non-TNBC, reported that the patient who develop recurrence, out of them 67.5% present within first 24 months of treatment, 16.2% within 2-3 years, and 16.2% from 3-6 years of primary treatment.

# CONCLUSION

Recurrence is very common within first 12 months after primary treatment in patients with triple negative breast cancer. In present study, recurrence occurred in 80% patients after primary treatment. Loco-regional recurrence occurred in 65% patients and all of the patients presented with distant metastasis.

**Author's Contribution:**

| | |
|---|---|
| Concept & Design of Study: | Sarah Khan |
| Drafting: | Ahmed Ijaz Masood |
| Data Analysis: | Zil-e-Huma |
| Revisiting Critically: | Sarah Khan, Ahmed Ijaz Masood |
| Final Approval of version: | Sarah Khan |

**Conflict of Interest:** The study has no conflict of interest to declare by any author.

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