



RESEARCH ARTICLE

TRIPLE NEGATIVE BREAST CANCER- EXPERIENCE AT TERTIARY CARE CENTRE, SOUTH INDIA

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ABSTRACT

Background: Triple negative breast carcinoma (TNBC), defined as tumors negative for ER, PR and Her 2 Neu receptors with distinct clinical entity characterised by aggressive behaviour, no specific targeted therapy and poor outcome.

Aims and objectives:

1. To study clinicopathological variable in TNBC
2. To study outcome of different modalities of management in TNBC.

Materials and Methods: A retrospective study was conducted based on hospital records in Department of General Surgery between March 2012 and October 2014. Inclusion criteria: All female patients with breast cancer who were treated in ESIC who had triple negative hormone receptors. Exclusion Criteria: No follow up records in cancer registry. Demography, Stage of disease at presentation, Management, response to neoadjuvant chemotherapy, Grade of tumour and follow up for 20 months were analyzed.

All patients underwent either modified radical mastectomy, breast conservative surgery as standard of care depending of stage of disease and anthracycline based chemotherapy was used for neoadjuvant or adjuvant setting.

Results: Out of 40 cases in the study period 30 cases (75%) belonged to age less than 45 years. Thirty two patients (82%) had premenopausal status. Predominant cases were in advanced stage. Out of 16 cases who received neo-adjuvant chemotherapy 100% response was noted with complete response rate at 13%. Infiltration ductal carcinoma was most common histology noted and 60% had grade 3 tumor. At mean follow up of 20 months, recurrence rate was noted in 11% of cases.

Conclusion: TNBC patients present at early age with high grade and advanced stage. Anthracycline based chemotherapy has excelled response when used in neoadjuvant settings.

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INTRODUCTION

Increasing burden of breast cancer has led to change in the treatment strategies, discovery of specific prognostic and predictive biomarkers. Hormone receptor testing has helped in individualized targeted therapies following Estrogen receptor (ER) positivity predicts response to endocrine therapy such as antiestrogen (tamoxifen), HER2/neu overexpression - Trastuzumab therapy (Herceptin). Based on molecular markers (ER, PR and HER2/ neu) and cytokeratin subtypes (CK 5&6, EGFR). Recent gene expression profiling studies have provided newer insight into the classification of breast cancer into:- A)ER positive -Luminal A & Luminal B B)ER negative-HER2/neu expressing, Basal like tumor & Unclassified Basal like phenotype is of major concern nowadays. It accounts for 10-20% of breast cancer cases.

Most of these are ER, PR and HER2/neu negative (approx. 75%), also referred to as Triple negative breast cancer. They are associated with aggressive behaviour of the tumor, poor clinical outcome, BRCA1 mutation, unresponsive to usual endocrine therapies, Shorter survival and Lack of targeted therapy. Combined chemotherapy is the present treatment modality.

Aims and objectives

- To study clinicopathological variable in TNBC
- To study outcome of different modalities of management in TNBC.

MATERIALS AND METHODS

A retrospective study was conducted based on hospital records in Department of General Surgery between March 2012 and October 2014. Inclusion criteria: All female patients with breast cancer who were treated in ESIC who had triple negative hormone receptors.

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Exclusion Criteria: No follow up records in cancer registry. Sample Size was estimated from available hospital statistics. Demography, Stage of disease at presentation, Management, response to neoadjuvant chemotherapy, Grade of tumour and follow up for 20 months were analyzed. Statistical data was expressed as Mean \pm SD. All patients underwent modified radical mastectomy as standard of care and anthracycline based chemotherapy was used for neoadjuvant or adjuvant setting.

RESULTS

The study consisted of 40 cases for TNBC during the study period and considered for analysis.

Table 1. Showing the age distribution of TNBC

Age group	Number of patients
<45 years	30
>45 years	10

Out of 40 cases in the study period 30 cases(75%) belonged to age less than 45 years. The difference in age group was statistically significant ($p < 0.05$). Thirty two patients (82%) had premenopausal status.

Table 2. Showing the treatment offered to TNBC patients

Treatment offered	Number of patients
Modified radical mastectomy f/b ct-rt	18 (45%)
Nact-mrm f/b ct-rt	16 (40%)
Palliative ct-rt	2 (5%)
Breast conserving surgery f/b ct-rt	4 (10%)

Table 3. Showing the NACT treatment response of TNBC patients

Response to nact	Number of patients (16)
Complete response	2 (13%)
Partial response	14 (87%)

Predominant cases were in advanced stage (16 cases). Out of 16 cases who received neo-adjuvant chemotherapy 100% response was noted with complete response rate at 13%.

Table 4. Showing the Gade of tumor of TNBC patients

Grade	NUMBER OF PATIENTS (40)
Grade I	5 (12.5%)
Grade II	12 (30%)
Grade III	23 (57.5%)

Infiltrative ductal carcinoma was most common histology noted and 57.5% had grade 3 tumor.

Histology	NUMBER OF PATIENTS (40)
Infiltration ductal carcinoma	35 (87.5%)
Infiltration lobular carcinoma	4 (10%)
Others	1(2.5%)

At mean follow up of 20 months, recurrence rate was noted in 11% of cases. Distant metastasis in 4 patients. Two patients has brain metastasis, Other two developed mets in liver, bone and lungs.

DISCUSSION

Our retrospective analysis was conducted in a 40 patients treated in the routine clinical practice with the median follow-up time of 20 months.

Emerging data on the clinical implication of the triple-negative phenotype indicate an aggressive course of this disease (Cummings *et al.*, 2011). In our study TNBC accounted for 20% of breast cancer with median age at presentation was 38 yrs with predominate cases under 45yrs of age and premenopausal (Cheang *et al.*, 2008; Iwase *et al.*, 2010; Li *et al.*, 2013). Similar to our study also other investigators found that characteristically TNBC exhibit an invasive ductal histology and a high histologic grade, present with high mitotic index, frequent apoptotic cells and carry central necrotic zones and pushing borders as well as a conspicuous lymphocytic infiltrate.^{4,5} Advanced disease at presentation is less compared to other studies attributable to awareness programmes conducted routinely for employees. Majority of tumors were more than 2cm in size and half of the patients had axillary nodal metastasis. Also in some previous reports triple negative tumours were described as relatively large tumours (>2cm) with a high rate of node positivity. 100% of the cases responded to anthracycline based NACT with complete response rate of 13% comparable to other studies. TNBC paradoxically demonstrates a higher response rate to neoadjuvant chemotherapy (Carey *et al.*, 2006). The results from published literature showed that patients with TNBC have an increased likelihood of distant recurrence and of death compared to women with other types of breast cancer. Mean follow up was for 18 months where 4 cases (11%) of stage 3 showed recurrence in bone, brain, lungs, liver etc. Metastatic stage4 cases survived for 2 & 4months post diagnosis suggesting the aggressive nature of TNBC.

Conclusion

TNBC presents in the younger age group with large and high grade tumors, and more difficult to treat. Locally advanced TNBC should be considered for NACT as patients with pathological complete response (pCR) have prolonged survival. High metastatic and recurrence rates emphasizes the need for identification of new biological markers and help to develop appropriate targeted therapy.

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