

Clinicopathological features of triple negative breast carcinoma- An experience from a tertiary care hospital.

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Abstract

Introduction: Triple negative breast cancers (TNBC) are defined as tumors that are negative for estrogen and progesterone receptors as assessed by immunohistochemistry (IHC) combined with lack of overexpression of HER2 when tested by IHC or absence of its gene amplification when tested by fluorescence in situ hybridisation technique. They are associated with poor prognosis. Triple negative breast cancers have an aggressive behaviour and wide metastasis. **Aim:** The aim was to study the clinicopathological features of TNBCs and compare them with non-TNBC tumors. **Materials and methods:** A retrospective study was conducted on 116 cases of breast carcinoma received during the period of 3 years. The tumor was classified based on immunohistochemical staining into three subtypes. The clinical details, histomorphological and immunohistochemical features of TNBCs were studied. **Results:** Out of the 116 patients, 28 patients were diagnosed as TNBC. The average age of presentation was 40 to 50 years. Most of the cases (96.5%) showed Nottingham Modification of Bloom Richardson grade 3. Lymph node metastasis was seen in 42% of cases. Unlike the other types of tumors, TNBC were mostly high grade. **Conclusion:** TNBCs have an aggressive behaviour compared to other subtypes with higher NMBR grade.

Key words- Breast carcinoma, TNBC, IHC.

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I. Introduction

Breast cancer is presently the second most common cancer in Indian women. By 2020, breast cancer is set to overtake cervical cancer as the most common type of cancer among all women in India¹. Breast cancer is a heterogeneous disease. It is classified according to its histologic pattern into various groups having different prognosis. While treating the patient the factors taken into account are histologic type, modified Bloom Richardson grade, TNM stage, estrogen and progesterone receptors status and overexpression of human epidermal growth factor receptor². The presence of ER and PR predicts that the cancer will respond to tamoxifen therapy and overexpression of Her2 predicts that the cancer will respond to trastuzumab (herceptin) therapy.

Gene expression profiling studies put a new insight into breast cancer classification beyond traditional histologic subtyping and grading. Breast tumors have been thus classified into three subtypes. These newly defined ER+veHer2 -ve, Her2 positive (ER+ve or ER-ve) and triple negative subtype of breast cancer in addition to being a powerful indicator of prognosis and also predictive of adjuvant hormonal and chemotherapeutic response^{3,4}.

Triple negative cancers are defined as tumors that are negative for estrogen and progesterone receptors as assessed by Immunohistochemistry (IHC) combined with lack of overexpression of Her2 when tested by IHC or absence of its gene amplification when tested by fluorescence in situ hybridisation technique. Hence these cancers do not respond to hormonal therapy and chemotherapy. These tumors form a distinct group because they affect younger patients and are more aggressive when compared with non-TNBC. TNBC often have a weak relationship between tumor size and node status. TNBC are the most distinctive group of breast cancers and they share a number of genetic similarities with serous ovarian carcinomas including the association of familial cancers of both types with germline BRCA1 mutations. These cancers can metastasize when small in size, frequently to viscera and to the brain. Local recurrence is common even after mastectomy.

An attempt was made to study the clinicopathological features of triple negative breast carcinoma by assessing histomorphological features of triple negative breast cancer, analysing various parameters such as age, site, tumor size, grade, stage and comparing these clinicopathological features in ER+veHer2-ve, Her2 Positive and Triple negative breast cancers.

II. Material And Methods

We studied invasive breast carcinoma, NOS specimens received in the dept of Pathology, KIMS, BBSR over a period of 3 years. The morphological parameters analysed were tumor size, histological grade, lymph node status and TNM stage. Immunohistochemical markers were identified such as Estrogen receptor (ER), Progesteron receptor (PR) and Her2 neu markers. The tumors were classified as A. ER+ve, Her2 -ve, B. Her2 positive (ER -ve or +ve) C. Triple negative breast cancers (ER-ve, PR-ve, Her2-ve). The clinicopathological details, histomorphological and immunohistochemical features among the other groups were compared. Various morphological features were analysed.

III. Results

In the present study 116 cases of breast cancer cases were reviewed of which 28 (24%) cases were triple negative breast cancers, 68 (58%) cases are Her2+ve and 20 (18%) cases are ER+ve, HER2-ve type. Among all the Her+ve cases 10 (8%) cases are Her2+ve, ER+ve and 58 (50%) cases are Her+ve, ER-ve. (Table-1).

Types	ER+ve, Her2-ve	Her2 +ve ER +ve	Her2 +ve ER-ve	Triple Negative
Percentage	20(18%)	10(8%)	58(50%)	28(24%)

Table 1: Comparison of triple negative breast cancers and tumors of other subtypes

Out of the 28 cases of TNBC the average age of clinical presentation was 40-50 years with minimum age being 23 yrs and maximum age being 58 yrs. Most of the cases (24/28) are in T2 category (size 2cm-5cm) and (4/28) cases are in T3 categories (size >5cm). None of the cases are in T1 category. 12/28 (42%) of tumors showed lymph node metastasis. NMBR grading was done on TNBC which showed 96.5% (27/28) of tumors were high grade (Grade-III). None of the tumors in our series are in grade I and 1 case (3.5%) in grade II. 16/28 (57%) of cases are in stage II and 12/28 (42%) cases are in stage III. None of the cases are in stage I. (Table-2)

Table-2. Clinical and histopathological features of patients with triple negative breast carcinomas (TNBC).

Parameters		N=28	Percentage%
Nuclear grade	Low	0	0
	Intermediate	1	3.5%
	High	27	96.5%
LN metastasis	Present	12	42.85
	Absent	16	57.15
Stage (TNM)	I	0	0
	II	16	57.15
	III	12	42.85
	IV	0	0
Size	T1	0	0
	T2	24	85.72
	T3	4	14.28
Age	20-30	1	3.5
	30-40	4	14.2
	40-50	20	71.4
	50-60	3	10.7
	60-70	0	0

IV. Discussion

Breast cancer is a heterogeneous disease encompassing numerous distinct histologic and gene profile based subtypes. Triple negative breast cancer represent one of the most aggressive phenotype with discrete risk factors and ominous prognostic significance. The current study revealed that immunohistochemical expression of various receptors such as ER, PR, Her2 neu which can relate to adverse pathological outcomes of the patients which are demonstrated in the prognostic indicators such as nuclear grade, lymph node metastasis and stage of the tumor.

Out of the 28 cases of TNBC the average age of the patient was 40-50 years. The mean age of the present study was comparable to earlier similar studies. The minimum age was 26 yrs in the present study similar to the age reported by Hasmi et al, Ishikawat et al and Qui et al. Qui et al found a higher incidence of familial

breast carcinoma in TNBC patients. In comparison with various Indian studies, the present study equated to the mean age of TNBC is 44-48 yrs of age. According to Suresh et al with study population of 171 TNBC cases, the mean age is 49 years was similar to the current study. Hence the present study correlates to various other studies that have been conducted on the similar focus of analysis.

Out of the 28 cases of triple negative breast tumors, 97% of the tumors are high grade. One of the study done by Ishikawa et al showed 91.8% of TNBC are in high grade (TABLE-3).

Nuclear grade	Ishikawa et al ⁵ ,2011 n-	Suresh et al ⁶ ,2013 n-128	Hashmi et al ⁷ ,2014 n-205	Fayaz et al ⁸ ,2014 n-320	Dogra et al ⁹ ,2014 n-67	Nabi et al ¹⁰ ,2016 n-62	Gowry et al ¹¹ ,2017 n-34	Present study n-116
Grade-I	2.1%	12.5%	4.9%	10%	1.5%	4.8%	5.9%	0
Grade-II	6.1%	26.5%	31.7%	33%	28.4%	38.7%	38.2%	3.5%
Grade-III	91.8%	61%	63.4%	57%	70.1%	56.5%	55.9%	96.5%

Table-3: Comparison of nuclear grading of Triple negative breast carcinomas among different studies.

Types	Percentage	Age(mean)	Tumor size	Stage	Grade
Her negative	18	52	T2	II	III(60%)
Her2 positive	58	24	T2	II	II(62%)
Triple negative	24	44	T2	II	III(96.5%)

Table-4: Comparison of Triple negative breast tumors and tumors of other subtypes in the present study.

Compared to triple negative tumors, 60% of HER2 -ve tumors were grade III with 52 years being the mean age of presentation and majority with absent distant metastasis.

Her2 neu positive tumors have a mean age of 24 yrs. Like TNBC tumors majority of the patients with Her2+ve type tumors presented with stage 2 but most of them are in grade II.

Triple negative breast cancers received various treatments such as modified radical mastectomy, chemotherapeutic measures such as paclitaxel and other treatment to treat underlying infections during therapy. Most of the patients with TNBC underwent multiple treatments and cycles of chemotherapy due to poor prognosis.

LIMITATION

In cases of equivocal Her2 Neu positive cases fluorescent in situ hybridisation (FISH) studies could not be done for confirmation due to financial issues.

V. Conclusion

Triple negative breast carcinomas encompass small proportion of breast cancer which shows negativity to estrogen, progesterone and Her2 neu. They are high grade carcinomas and less likely to respond hormonal and transzumabtherapy. Hence they are known to demonstrate poor prognosis.

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