

PROGNOSTIC FACTORS AND SURVIVAL IN TRIPLE NEGATIVE AND NON-TRIPLE NEGATIVE BREAST CANCER: EXPERIENCE OF A TERTIARY CARE CANCER CENTER IN ODISHA.

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Abstract

Background: Because of its high-risk biological features and lack of effective treatment options, triple-negative breast cancer (TNBC) has received greater clinical and experimental interest.

Aim and objectives: The aim of this study was to compare and analyze the clinicopathological features, recurrence, metastasis, and prognosis of patients with TNBC and non-triple negative breast cancer (non-TNBC).

Material and methods: This single hospital-based retrospective study was conducted on patients who were histopathologically diagnosed with breast cancer and subsequently treated from 2017 to 2018 at the Acharya Harihar Postgraduate Institute of Cancer. The clinical features and prognosis of TNBC and non-TNBC were compared.

Results: This study comprised a total of 111 patients, with 36 (32.43%) being TNBC and 75 (67.56%) being non-TNBC. TNBC has 22 patients under the age of 40 (61.1%). Grade III tumors were seen in 47% of TNBC patients and 21% of non-TNBC patients (p-value = 0.05). The disease free survival (DFS) was determined to be 58 % for TNBC and 82% for non-TNBC groups, respectively (p-value = 0.05). These two groups had an overall survival rate (OS) of 72% and 92%, respectively (p-value = 0.05).

Conclusion: When compared to non-TNBC, TNBC was related to high-grade malignancies, worse disease-free survival, and overall survival (OS) rates. Understanding the molecular features of TNBC, clarifying its mechanism at the molecular level, interpreting the gene expression profiles of TNBC, and studying and creating new therapeutic targets should be the focus of future research. To enhance the prognosis of TNBC patients, try to find a focused and effective therapy.

Keywords: Breast cancer; survival; triple-negative breast cancer..

Introduction

Breast cancer (BC) is a complex disease with many different biological and clinical characteristics. It is the most common cancer among women worldwide, accounting for 25% of all cancer cases. According to Globocan 2020, the global incidence and mortality of breast cancer were 2,261,419 new cases and 684,996 deaths. In 2020, India recorded 178 361 new cases, with 90408 deaths. [1]

Prognostic and predictive factors have long been used to guide treatment decisions for breast cancer. Aspects to examine include the degree of axillary lymph node involvement, histopathologic grade, patient age, lymphatic or microvascular space involvement, hormone receptor status, and human epidermal growth factor receptor-2 (HER-2/neu). [2]

TNBC is a form of breast cancer that lacks the estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 (HER-2) and has high invasiveness, high metastatic potential, recurrence tendency, and a poor prognosis. Because TNBC tumors lack ER, PR, or HER2 expression, they are not sensitive to endocrine therapy or HER2 treatment, and there are presently no standardized TNBC treatment regimens. [3] So this subtype, has attracted more clinical and experimental attention. [4]

TNBC is more common in India (31%) than it is in Western nations (12.2%–13%). [5] The high occurrence of TNBC in the Indian population has been linked to a number of risk factors, the most prominent of which include lifestyle, socioeconomic status, obesity, family history, high mitotic

indices, and BRCA1 mutations. Due to a lack of targeted medicines, the treatment of TNBC is severely impeded. [6]

In India, there is a lot of heterogeneity in TNBC prevalence across different studies. Breast cancer is one of the most common malignancies among women in Odisha (accounting for 26% of all malignancies), with a significant prevalence of triple-negative breast cancer patients (47.9%).[7-8]

The researchers wanted to compare and contrast the clinicopathological features, recurrence, metastasis, and prognosis of TNBC and non-triple negative breast cancer patients in this study (non-TNBC).

Materials and methods:

This single hospital-based retrospective study was conducted on patients who were histopathologically diagnosed with breast cancer and subsequently treated from 2017 to 2018 at the Acharya Harihar Postgraduate Institute of Cancer.

Inclusion Criteria:

- Patients with pathologically proven breast cancer.
- Cases with complete clinical, pathological, and follow-up data

Exclusion criteria:

- Patients with incomplete clinical details.
- Those patients in whom there is no/incomplete information about ER/PR and HER-2 neu status.
- Patients who had received neoadjuvant chemotherapy were also excluded from the present study.

Patients' clinical histories, tumor characteristics, ER, PR, and HER2 status, therapy, and recurrence, among other things, were compiled using clinical records. All of the data was collected in compliance with data privacy guidelines.

Patients were followed up from the time they underwent surgery until they died, or until October 31, 2021. The

average time of follow-up was 23 months (a range of 13–46 months).

The status of ER, PR, and HER2 was determined using immunohistochemistry (IHC) and/or fluorescence in situ hybridization (FISH). The sample was considered negative for ER or PgR if fewer than 1% or none of the tumor cell nuclei were immunoreactive. The HER2/neu was evaluated on a qualitative scale of 0 to 3+ based on the strength of membranous staining, with 0 and 1+ indicating negative, 2+ suggesting borderline, and 3+ indicating positive. FISH analysis was utilized to re-evaluate HER2 (++) tissues, and the tissue was termed HER2/neu positive if the HER2 gene amplification copy-to-CEP17 ratio was greater than 2.0.

Statistics: Means (standard deviation [SD]) or medians were used to present quantitative data, whereas frequencies or proportions (range) were used to present qualitative data. Using a 2-test for frequencies, we compared the demographics and tumor features of patients with TNBC versus non-triple-negative breast cancer. P-values were two-sided in all analyses, and p-values less than 0.05 were deemed statistically significant. IBM SPSS software was used to conduct the aforementioned statistical analyses (Version 23, SPSS Inc, Chicago, IL, USA).

Results:

The study included 111 individuals, with 36 (32.43 percent) having TNBC and 75 (67.56 percent) having non-TNBC. The median ages of TNBCs and non-TNBCs were 44 (26-66) and 46 (33–72) years, respectively. Twenty-two TNBC patients (61.1%) were beyond the age of 40, compared to twenty-four non-TNBC patients (38.9%). The distribution of patient features into two groups is depicted in [Table 1].

The DFS for TNBC and non-TNBC groups was calculated to be 58 percent and 82 percent, respectively, which was statistically significant (p value=0.05). The OS of these two groups was significantly different (p value=0.05). The frequency of recurrences and metastasis sites are shown in [Table 2].

Table 1: Distribution of various patient characteristics.

Prognostic Factors		Total Cases n=111 (100%)	TNBC n=36 (32.43%)	Non-TNBC n=75 (67.56%)	P value
Age	≤40	46(41.44)	22(61.11)	24(32)	.003*
	≥41	65 (58.55)	14(38.88)	51(68)	
Tumor type	IDC	106(95.49)	34(94.44)	72(96)	.711
	Others	5(4.50)	2(5.55)	3(4)	
Grade	I & II	78(70.27)	19(52.77)	59(78.66)	.005*
	III	33(29.72)	17(47.22)	16(21.33)	
LVSI	Present	39(35.13)	18(50)	21(28)	.458
	Absent	72(64.86)	28(77.77)	44(58.66)	
PNI	Present	23(20.72)	7(19.44)	16(21.33)	.818

	Absent	88(79.27)	29(80.55)	59(78.66)	
Tumor stage	T1	4(3.6)	2(5.55)	2(2.66)	.746
	T2	82(73.87)	26(72.22)	56(74.66)	
	T3	25(22.52)	8(22.22)	17(22.66)	
Node stage	N0	39(43.24)	12 (58.33)	27 (36)	.154
	N1	38(34.23)	10(27.77)	28(37.33)	
	N2	19(12.61)	8(8.33)	11(14.66)	
	N3	15(9.9)	6(5.55)	9(12)	
Local Recurrence	Yes	3(2.7)	1(2.77)	2(2.66)	.973
	No	108(97.29)	35(97.22)	73(97.33)	
Distant recurrence	Yes	25(22.52)	14(38.88)	11(14.66)	.004*
	No	86(77.47)	22(61.11)	64(85.33)	
Death	Yes	16(14.41)	10(27.77)	6(8)	.005*
	No	95(85.58)	26(72.22)	69(92)	
DFS		83(74.7)	58%	82%	.005 *
OS		95(85.5%)	26(72.2%)	69(99.2%)	.005*

LVSI:Lymphovascular stromal invasion;PNI:Perineural Invasion;IDC:Invasive duct carcinoma;* showing significant (p-value <0.05)

Table 2: The frequency of recurrences and metastasis sites.

Metastasis to Organ	Total	TNBC	Non- TNBC
Brain	3	1	2
Bone	5	2	2
Lung	8	4	4
Liver	7	6	2
Other	5	2	3
Total	28 (25.22%)	15 (53.57%)	13 (46.42%)

Discussion:

This study indicated a greater rate of TNBC cases, which was consistent with other Indian studies. TNBC patients showed up at a younger age than non-TNBC patients did [9–10]. Other investigations have come up with similar results. [11]

Breast cancer that is triple-negative is linked to aggressive behaviour and a significant probability of local and regional failure. Surgical intervention that is aggressive is regarded as appropriate. [12]

In this context, Kim et al. [13] discovered that breast conservation remained a feasible option in patients with TNBC, with identical DFS and OS to mastectomy, in well-chosen individuals. Agarwal et al. [9] from India reported similar findings, finding that around 20% of patients in both the TNBC and non-TNBC groups required breast-conserving surgery. In this study, conservative breast surgery was performed 19.81 percent of the time.

Because of their higher grade, triple-negative tumors are more aggressive. In one of the largest studies on TNBC

from a single institution, the prevalence of Grade III tumors was 66 percent in TNBC patients and 28 percent in non-TNBC patients.[14]

When compared to non-TNBC, TNBC showed poorly differentiated tumors, with 78 percent vs. 46 percent (p 0.0001) in another study. [15] According to Lakshmaiah et al., TNBC patients develop high-grade malignancies in 88 % of cases. [16]

In this study, age and tumor grade, nodal yield were all statistically different between TNBC and non-TNBC, while pathological tumor size, nodal yield, lymphovascular invasion, and the number of positive nodes were not. Other research had similar results. [2,11,15]

However, Agarwal et al. [9] and Dent et al. [14] found that TNBC patients had a greater rate of nodal metastasis than non-TNBC patients. They also noted that, whereas there was an increased incidence of nodal involvement as tumor size grew in the non-TNBC subset of patients, this association was not apparent in the TNBC cohort, which

had an increased chance of being node-positive even at lower tumor sizes.

According to Lin et al. [17], women with triple-negative tumors were more likely to have their first recurrence in the brain, lung, or locoregional locations and were less likely to have their first recurrence in the bone. While the majority of recurrences were found to be in the lung and CNS by Dent et al. [14], only a handful were preceded by locoregional recurrences.

Suresh et al. [18] found 34 recurrences in 171 TNBC patients with a median follow-up of 30 months. There were 25 systemic relapses, with lung and CNS relapses (13), about four times as prevalent as bone relapses (three).

Patients with TNBC had a shorter life expectancy than other breast cancer subtypes, with a mortality rate of 40% in the first five years after diagnosis. [3]

Although the frequency of locoregional failures, distant failures, and mortalities was not statistically different in prior investigations, the DFS, remote failures, and overall survival of the two groups were significantly different in this investigation. Overall survival (78.1% vs. 83.0%, $p = 0.2$) and 5-year disease-free survival (75.0% vs. 74%, $p = 0.7$) did not differ statistically. [12]

According to other research, TNBC had a 2-year overall and disease-free survival rate of 52.1 percent and 43.5 percent, respectively, compared to 83.8 percent and 73.4 percent for non-TNBC ($P.001$). [19]

Conclusion

When compared to non-TNBC, TNBC was related to younger age, high-grade malignancies, worse disease-free survival (DFS), and overall survival (OS) rates. Understanding the molecular biology features of TNBC, clarifying its mechanism at the molecular level, interpreting the gene expression profiles of TNBC, and studying and creating new therapeutic targets should be the focus of future research. To enhance the prognosis of TNBC patients, try to find a focused and effective therapy.

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