

Outcome of Triple Negative Breast Cancer(TNBC) as compared to other breast cancers in Bir Hospital, National Academy of Medical Sciences

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Abstract

Introduction: In Nepal, breast cancer is the second most common cancer accounting for a large number of deaths. The subtype Triple-negative breast cancer (TNBC) is linked to poor prognosis and is characterized by the absence of estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor-2 (HER2). This study describes the outcome of women with TNBC as compared to other breast cancers in Bir Hospital in Nepal.

Methods: This was a cross-sectional study conducted in Bir Hospital, National Academy of Medical Sciences. The breast cancer data in Department of Surgery and Department of Oncology were collected from July 2021 to June 2024. The study data on demographic details, clinical findings, radiological and pathological investigations, operative procedures, neoadjuvant/adjuvant therapy, surgical and oncological outcomes were collected. The study approval was taken from Institutional Review Board of National Academy of Medical Sciences.

Results: There were 72 breast cancer patients out of which 10 (13.8 %) were TNBC. Majority of the cases (70%) underwent modified radical mastectomy and 60% of them had received neoadjuvant therapy in TNBC cases. One out of 10 had positive margin post mastectomy. The proportion of TNBC patients with postoperative wound infection, seroma and flap necrosis were 10% each. The mean lymph node positivity was less in TNBC group as compared to other breast cancers. There was one recurrence, one metastasis and no mortality till one year follow up.

Conclusion: The surgical outcome was satisfactory and with neoadjuvant, surgery and adjuvant therapy, there is less tumor recurrence and satisfactory disease free survival and overall survival.

Keywords: Breast cancer; outcome; TNBC.

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Introduction

Breast cancer is the most prevalent cancer among women, characterized by significant heterogeneity. This diversity in the disease leads to considerable differences in clinical management and outcomes among patients. The most prevalent subtype of breast cancer, accounting for 73% of cases, is characterized by positive estrogen receptors (ER) or progesterone receptors (PR) and negative human epidermal growth factor receptor 2 (HER2).¹ This subtype is associated with the most favorable prognosis. Conversely, Triple-negative breast cancer (TNBC) is characterized by the absence of estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor-2 (HER2) expression, comprises 12% of breast cancer cases and is linked to the poorest prognosis.¹

Epidemiological studies indicate TNBC predominantly affects premenopausal women under 40 years old, and those with low socioeconomic status.^{2,3} Incidence is higher in South Asian countries (35.2%) compared to that of the West (12.2% to 24%) but less when compared to that of African countries (45.7%).^{4,5} TNBC is positively associated with reproductive factors such as early menarche and high parity.^{6,7} The BRCA1 protein regulates DNA repair, transcriptional activation, cell cycle regulation, and chromatin remodeling, while the BRCA2 protein is involved in transcriptional and cell cycle regulation, DNA repair, mitophagy, and the stabilization of the replication fork.⁸ It has been suggested that BRCA mutations exist in around 10–15% of TNBC patients. In addition, about 48% of people with BRCA 1 mutations developed TNBC.⁹

In Nepal, breast cancer is the second most common cancer after lung, accounting for 10.2% of all cancer cases and the age-standardized mortality rate for breast cancer in Nepal is 7.8 per 100,000 women, with an estimated 1,149 deaths in 2022.¹⁰ The 5-year survival rate for breast cancer in Nepal is lower compared to developed countries, likely due to delayed diagnosis and limited access to optimal treatment.¹¹ Prevalence of TNBC in South Asia is reported to be higher than that observed in Western populations; however, there is considerable variation in prevalence rates reported by studies from the region. This study aims to find out the prevalence, profile and outcome of TNBC to other types of breast cancer in Bir Hospital in Nepal.

Methods

This was a cross-sectional study conducted in Bir Hospital, National Academy of Medical Sciences. Bir Hospital is a central government hospital of Ministry of Health and Population of Nepal under National Academy of Medical Sciences in Kathmandu, Nepal. The study population was breast cancer patients presenting to Department of Surgery and Department of Oncology in Bir Hospital, National Academy of Medical Sciences. The triple negative breast cancer patients (TNBC) were breast cancer patients with all three hormone status – estrogen receptor, progesterone receptor and Her-2 neu receptor negative assessed by

Immunohistochemistry. The data of breast cancer who presented to outpatient clinics in Department of Surgery or Department of Oncology in Bir Hospital, National Academy of Medical Sciences who fulfilled the inclusion criteria were collected by data collectors from the hospital records from July 2021 to June 2024. The sampling technique was convenience sample. The inclusion criteria were patients of age more than 18 years, patients with diagnosis of breast cancer (any stage) who underwent treatment in Bir Hospital and breast cancer patients who regularly followed up in Bir Hospital. The exclusion criteria were breast cancer patients diagnosed in Bir Hospital and treated in other hospitals and breast cancer patients who did not follow up in Bir Hospital. The data collectors (surgeons, oncologists, nurses) were oriented about research objectives, variables and data collection techniques in Microsoft Excel. Each case was identified by “case number” and patient’s identification details were not collected. The study data on demographic details, clinical finding (patient demography, clinical symptoms, breast and axilla examination findings), radiological and pathological investigations, operative procedure and findings, neoadjuvant/adjuvant therapy, surgical and oncological outcome were collected from hospital records. The surgical complication data of breast cancer patients (wound infection, seroma formation and flap necrosis) were collected till 28 days following surgical procedure for breast cancer as per Clavien Dindo classification. The data on margin positivity, number of axillary lymph nodes, recurrence and survival were taken from hospital records.

The operation definition for oncologic outcome from six months to three years follow up were as follows- Ipsilateral Breast Tumor Recurrence (IBTR)- the percentage of patients with ipsi-lateral local recurrence of breast carcinoma, Disease Free Survival (DFS)- the percentage of patients being alive without having had any breast cancer recurrence (i.e., local, regional, contralateral, or distant), Overall Survival(OS) the percentage of patients being alive.

The interim data analysis was performed on the variables of surgical site infection, flap necrosis, wound seroma, margin positivity and oncologic outcomes. The study approval was taken from Institutional Review Board of National Academy of Medical Sciences.

Results

Out of 72 breast cancer patients, 10(13.8%) patients were TNBC. The age of presentation of TNBC was 43.4± 9.1 years and all were female. Five TNBC patients were from Kathmandu, three from Nuwakot and one each from Bajura and Makwanpur. Six were left breast and four were right breast cancers. Five patients were more than BIRADS 4. Majority of the cases (70%) underwent modified radical mastectomy. The histopathologies of 40% were invasive breast carcinoma, 20% ductal carcinoma and 10% medullary type and pleomorphic type each. Six patients

Table 1. Comparison of demography, clinical, radiological, histopathological findings and treatment between TNBC and Non-TNBC

	TNBC (n=10)	Non-TNBC (n=62)
Prevalence	10(13.8%)	62(86.2%)
Age at presentation (mean±SD years)	43.4± 9.1	47.3±9.7
Sex		
Female	10(100%)	59(95.1%)
Male	0	3(4.8%)
Geographical distribution (Province)		
Koshi	0	9(14.5%)
Madhesh	0	2(3.2%)
Bagmati	9(90%)	24(38.7%)
Gandaki	0	2(3.2%)
Lumbini	0	3(4.8%)
Karnali	1(10%)	0
Sudurpaschim	0	1(1.6%)
Laterality		
Left	60%	56.5%
Right	40%	43.5%
Symptoms at presentation		
Breast lump	60%	67.7%
Others (ulcer, discharge, pain)	40%	32.3%
BIRADS		
0	1(10%)	1(1.6%)
I	0	1(1.6%)
II	0	3(4.8%)
III	0	3(4.8%)
IV	1(10%)	16(25.2%)
V	4(40%)	10(16.1%)
VI	0	1(1.6%)
Neoadjuvant therapy	6(60%)	8(12.9%)
Surgery		
Modified radical mastectomy	70%	50%
Breast conserving surgery with axillary dissection	0	1(1.6%)
Toilet mastectomy	0	1(1.6%)
Adjuvant therapy	40%	20.9%
Histopathology (WHO classification 2019)¹²		
Invasive breast carcinoma(NST)	40%	33.8%
Infiltrating duct carcinoma (NOS)	20%	14.5%
Lobular carcinoma(NOS)	0	3.2%
Mixed (ductal with lobular) carcinoma	0	1.6%
Metaplastic carcinoma (NOS)	0	0
Metastatic carcinoma	10%	0
Papillary carcinoma	0	1.6%
Medullary carcinoma	10%	0
Mixed (ductal with lobular) carcinoma	0	1.6%

received neo adjuvant therapy and four received adjuvant therapy (Table 1).

In TNBC group, one out of 10 had positive margin with (<0.1cm) post mastectomy. The proportion of TNBC patients with post operative wound infection, seroma and flap necrosis were 10% each. The mean lymph node positivity was less in TNBC group as compared to other breast cancers, 0.9± 2.4 vs 4.6±5.9 respectively. (Table 2)

Table 2. Comparison of Surgical outcome between TNBC and Non-TNBC

Surgical outcome		TNBC (n=10)	Non-TNBC (n=62)
Wound complications	Wound Infection	1(10%)	3(4.8%)
	Seroma	1(10%)	1(1.6%)
	Flap Necrosis	1(10%)	3(4.8%)
Margin positivity		1(10%)	1(1.6%)
Lymph node status	Mean axillary lymph node harvested	11.2 ± 6.8	15.3±6.6
	Lymph node positive	0.9± 2.4	4.6±5.9
Need of post operative blood transfusion		0	0

There was one recurrence and no mortality till one year follow up. One out of 9 patients had lung metastasis in TNBC group. In non-TNBC group, one patient had supraclavicular recurrence and two patients had ipsilateral breast tumor recurrence. (Table 3)

Table 3. Comparison of Oncologic outcome (Breast cancer recurrence and survival)

Oncologic outcome	TNBC (n=10)	Non-TNBC (n=62)
Ipsilateral breast tumor recurrence (IBTR)	1(10%)	2(3.2%)
Disease Free survival(DFS)	9(90%)	59(95.1%)
Overall survival(OS)	10(100%)	

Discussion

Triple-negative cancers are notably aggressive tumors with unique epidemiological, pathological, and prognostic features.¹³ In our study, TNBC accounted for 13.8% of breast cancer which is less than other South Asian countries but similar to that of Western countries. Geographically, TNBC patients were more frequently found in the Bagmati province, which was high as compared to other provinces of Nepal. This can be due to easy access for patients in Bagmati province to visit Bir Hospital and referrals to Bir Hospital from other hospitals in the province.

Compared to other breast cancer subtypes, TNBC is associated with a shorter survival time, with a 40% mortality

rate within the first five years post-diagnosis.¹³ In our study, there was 100% survival in one year follow up with one patient having ipsilateral tumor recurrence. The median survival time after metastasis is around 13.3 months, and the recurrence rate following surgery is about 25%, frequently involving the brain and visceral organs. Metastasis typically occurs in the third year after diagnosis.¹⁴ TNBC is notably aggressive, with approximately 46% of patients experiencing distant metastasis where as in our study, one patient had lung metastasis. In our study, follow up is short to provide long term prognosis.

Initial treatment of TNBC seems successful and cancer cells seem receptive to primary chemotherapy. In our study, six patients had received neo-adjuvant therapy and four patients had received adjuvant therapy. Due to its unique molecular characteristics, TNBC does not respond well to endocrine or targeted molecular therapies, making chemotherapy the primary systemic treatment. However, conventional adjuvant chemoradiotherapy has limited effectiveness, often leading to tumor recurrence from residual metastatic lesions.¹⁵ There are studies which have found TNBC to be highly responsive

to chemotherapy, exhibiting higher rates of pathological complete response (pCR) compared to hormone receptor-positive tumors.¹⁶ Regardless of the surgical approach, recurrences are primarily systemic, with local relapses being exceedingly rare.

Conclusion

In TNBC, the surgical outcome was satisfactory and with neo-adjuvant, surgery and adjuvant therapy the tumor recurrence is low along with satisfactory disease free survival and overall survival in short-term follow up. The management of TNBC at Bir hospital conforms with international standards.

Disclaimer:

No conflict of interest. Where authors are identified as personnel of the International Agency for Research on Cancer/World Health Organization, the authors alone are responsible for the views expressed in this article and they do not necessarily represent the decisions, policy, or views of the International Agency for Research on Cancer/World Health Organization.

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