Pattern of Breast cancer: A study from western Nepal

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Abstract

Introduction: Breast cancer is the most common cancer among females, accounting for 18.5% of cases globally. It is a heterogeneous disease with varying clinical, pathological, and molecular features. Molecular classification into Luminal A, Luminal B, HER2-enriched, and Triple-Negative subtypes, based on immunohistochemical markers (ER, PR, HER2, Ki-67), guides treatment decisions. Neoadjuvant therapy improves survival, particularly in Triple-Negative Breast Cancer (TNBC), and reduces surgical extent. This study analyzes breast cancer patterns at a tertiary care center to contribute to national data.

Methods: A descriptive cross-sectional study was conducted at Sushil Koirala Prakhar Cancer Hospital from January 2018 to January 2024. Data were collected from medical records and patients, including demographic details, risk factors, histopathology, TNM staging, and chemotherapy protocols. Immunohistochemistry classified molecular subtypes per St. Gallen Consensus 2011 guidelines. Statistical analysis was performed using SPSS version 23.

Results: A total of 166 breast cancer patients were studied, with a mean age of 51.2±12.79 years. Most were married (91%), and only 2.4% had a family history of breast cancer. Delayed treatment (>3 months) was observed in 60.8% of cases. The most common tumor stage was T3 (35.5%), and the most frequent molecular subtype was Luminal A (31.3%). Stage IIIA was predominant (33.1%). Estrogen receptor positivity was found in 57.2% of

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cases. The most used chemotherapy regimen was AC 2-weekly followed by 2-weekly paclitaxel (29.5%). The majority (63.3%) were referred cases from other institutions.

Conclusion: This study highlights that most breast cancer cases in western Nepal present at advanced stages, with delayed treatment initiation in a significant proportion. Luminal A was the predominant subtype, and chemotherapy with AC 2-weekly followed by paclitaxel was most commonly used

Key words: Breast Cancer, western Nepal, treatment, protocol

Introduction

According to GLOBOCAN 2022, breast cancer the most common cancer in females (18.5%) and the second most common in both sexes, causing 1,149 (7.8%) cancer-related deaths.[1] It is a heterogeneous disease with diverse clinical, pathological, molecular, and genetic features, leading to varied treatment responses and outcomes.[2] Clinical presentations range from painless breast lumps to advanced symptoms like axillary lumps, back pain, cough, and jaundice, depending on metastasis. Histologically, breast cancer includes 20 major types and 18 minor subtypes, each with distinct outcomes, as per the WHO classification.[3] Traditional classification based on morphology and clinical-pathological parameters is insufficient to predict tumor behavior. [4,5]

Molecular classification identifies four subtypes: Luminal A, Luminal B, HER2-enriched, and Triple-Negative, based on gene expression profiles.[6] Immunohistochemical markers (ER, PR, HER2, Ki-67) are crucial for stratifying these subtypes. [7,8] Treatment depends on TNM stage, hormone receptor status, and HER2 status, involving systemic therapy, surgery, radiotherapy, and targeted therapies. Neoadjuvant and adjuvant therapies show comparable survival outcomes, with hormone receptor status guiding chemotherapy decisions.[9,10] Pathologic complete response (pCR) to neoadjuvant therapy strongly correlates with improved survival, especially in Triple-Negative Breast Cancer (TNBC).[11,12] Neoadjuvant chemotherapy also reduces surgical extent and micrometastatic disease, enhancing quality of life.[13,14]

This study aims to analyze breast cancer patterns at a tertiary care center, contributing to national data and exploring the proportion of various cancer types.

Method:

A descriptive cross-sectional study was done at the Department of Medical Oncology at Sushil Koirala Prakhar Cancer Hospital (SKPCH) from January 2018 to January 2024. The study encompassed all patients diagnosed and/or treated for breast diseases, including breast cancer, at the Sushil Koirala Prakhar Cancer Hospital (SKPCH). As a tertiary referral center, SKPCH receives a majority of its breast cancer patients through referrals from physicians, other hospitals, or as self-referrals from various regions across the country. However, cases involving benign breast lesions or suspected breast cancers that lacked histological confirmation were excluded from the study.

The data were collected from hospital medical records and directly from patients after obtaining their consent. Information recorded included basic demographic details such as name, age, sex, and address, as well as risk factors like menstrual status (peri- or post-menopausal), use of hormonal therapy, obstetric history, and tobacco and alcohol consumption.Additionally, anthropometric measurements, histopathology findings, TNM staging, and chemotherapy protocols were documented.

Immunohistochemistry (IHC) was performed on representative tumor paraffin blocks following the St. Gallen Consensus 2011 guidelines. Using antibodies for ER, PR, HER2, and Ki67, breast cancers were classified into molecular subtypes, as outlined below, without the need for molecular diagnostics. This approach is advantageous, as IHC-based classification does not require an expensive, highly specialized laboratory.[2,8] Breast cancers were classified into four molecular subtypes based on immunohistochemistry results: Luminal A, characterized by ER+ and/or PR+ expression, HER2/neu negativity, and Ki67 < 14%; Luminal B, which includes two subgroups—HER2/neu negative (ER+ and/or PR+, HER2 negative, Ki67 ≥ 14%) and HER2/neu positive (ER+ and/or PR+, HER2 positive, with any Ki67 level); HER2-positive (non-luminal), defined by ER-, PR-, and HER2 positivity; and triple-negative, which is negative for ER, PR, and HER2 expression.

The identity and data of each patient were kept strictly confidential, with a unique code number assigned to ensure anonymity. All statistical analyses were conducted using SPSS version 23 (SPSS, Chicago, IL). Statistical tests were performed at a 95% confidence level and

were two-sided, with a p-value of less than 0.05 considered statistically significant. Descriptive statistics, including mean, median, mode, standard deviation (SD), and quartiles, were used to summarize quantitative data, while proportions were used for qualitative data.

Result:

Among a total of 166 patients. The mean age of patients was 51.20±12.794 years. Most participants were married 151 (91.0%), while a small proportion were unmarried (8, 4.8%), divorced (2, 1.2%), or widowed (5, 3.0%). A family history of breast cancer was reported in only 4 cases (2.4%), while 146 (88.0%) had no such history, and 14 (8.4%) did not provide this information. Regarding treatment timing, 54 patients (32.5%) sought treatment within 3 months of symptom onset, while 101 (60.8%) did so after 3 months, and 11 (6.6%) had missing data. In terms of tumor characteristics, T3 tumors were the most common (59, 35.5%), followed by T2 (42, 25.3%) and T4a (25, 15.1%). (Table 1)

The distribution of breast cancer cases across different age groups shows that the highest number of cases is in the 45-54 age group, with 51 (30.7%) cases. The 35-44 age group follows, accounting for 42 (25.3%) cases. The 55-64 and 65-74 age groups have 29 (17.5%) and 24 (14.5%) cases, respectively. (Table 1)

Table 1: Clinico-demographical Features of Patients with Breast Cancer (n=166).

Titles	Number (Percentage)
Age	
Mean	51.20
Median	51
Standard deviation	12.794
Range	19-82
Marital status	
Married	151 (91.0%)
Unmarried	8 (4.8%)
Divorced	2 (1.2%)
Widow	5 (3.0%)
Family history of breast cancer	
Not mentioned	14 (8.4%)
No	146 (88.0%)
Yes	4 (2.4%)
Personal history of breast related disease	
Yes	22 (13.3%)
No	130 (78.3%)
Not mentioned	14 (8.4%)
Time from symptom to treatment	
Up to 3 months	54 (32.5%)
>3 months	101 (60.8%)
Missing	11 (6.6%)
Alcohol history	
Missing	14 (8.4%)
No	124 (74.7%)
Yes	28 (16.9%)
Tobacco consumption	
Missing	11 (6.6%)
Yes	42 (25.3%)
No	113 (68.1%)
Laterality	
Right	75
Left	88
Both	3
T staging	
T1	14 (8.4%)
T2	42 (25.3%)
T3	59 (35.5%)
T4a	25 (15.1%)
T4b	9 (5.4%)
T4c	3 (1.8%)
T4d	12 (7.2%)

Table 1: Clinico-demographical Features of Patients with Breast Cancer (n=166).	
Titles	Number (Percentage)
T0	2 (1.2%)
N staging	
N0	18 (10.8%)
N1	65 (39.2%)
N2	72 (43.4%)
N3	11 (6.6%)
M staging	
M0	138 (83.1%)
M1	28 (16.9%)
Missing	7 (4.2%)

The distribution of breast cancer cases based on BMI shows that the majority of patients fall within the normal BMI range (17.5-22.99), with 70 (42.2%) cases. (Table 2)

The majority of the cases 105 (63.3%) were the referred cases from the different institutions, and 61 (36.7%) were the cases diagnosed in the Sushil Koirala Prakhar cancer hospital.

The most common pattern of presentation was a breast lump, observed in 156 (94%) cases, followed by an axillary lump in 72 (43%). Ulceration was noted in 24 (14%). Features of distant metastasis involving the bone, liver, brain, or lungs were present in 12 (7%) cases. Changes in the nipple, such as discharge or inversion, were seen in 9 (5%). Features of breast infection were noted in 5 (3%), with the majority being inflammatory breast carcinoma. (Table 3)

The distribution of breast cancer stages among patients is as follows: Stage I was observed in 4 (2.4%) cases. Stage IIA was present in 16 (9.6%) cases, while Stage IIB accounted for 19 (11.4%) cases. Stage IIIA was noted in 55 (33.1%) cases, and Stage IIIB in 39 (23.5%) cases. Stage IIIC was identified in 7 (4.2%) cases. Stage IV was seen in 26 (15.7%) cases.

Estrogen receptor positivity was observed in 95 (57.2%) of cases. Progesterone receptor positivity was noted in 84 (50.6%) of cases. HER2 receptor positivity was seen in 32 (19.3%) of cases. (Table 2)

Table 2: Hormone Status of Patients with Breast Cancer (n=166).					
Receptor Status	Negative n (%)	Positive n (%)	Equivocal n (%)	Couldn't Afford/Missing n (%)	Total n (%)
Estrogen Receptor (ER)	65 (39.2 %)	95 (57.2 %)	-	6 (3.6%)	166 (100 %)
Progesterone Receptor (PR)	76 (45.8 %)	84 (50.6 %)	-	6 (3.6%)	166 (100 %)
HER2 Receptor	118 (71.1 %)	32 (19.3 %)	10 (6.0%)	6 (3.6%)	166

The most prevalent molecular subtype was Luminal A 52 (31.3%), followed by Triple Negative 46 (27.7%), Luminal B HER2-negative 20 (12.0%), HER2-enriched 16 (9.6%), and Luminal B HER2-positive 14 (8.4%). A few patients, 2 (1.2%), had an unclassified status with ER-negative and PR-positive findings.

Table 3 : Classification of Breast Cancer according to Hormone Receptor Status (n=166).

Age Group (years)	Luminal A	Luminal B HER2-negative	Luminal B HER2-positive	HER2-enriched	TNBC	ER-, PR +ve	Couldn't be done	Total (%)
<25	0	0	0	0	3 [1.8%)	1 [0.6%)	1 [0.6%)	5 [3.0%)
25-34	0	0	1 (0.6%)	1 (0.6%)	5 (3.0%)	0	0	7 (4.2%)
35-44	10 (6.0%)	4 (2.4%)	2 (1.2%)	6 (3.6%)	18 (10.8%)	0	2 (1.2%)	42 (25.3%)
45-54	22 (13.3%)	7 (4.2%)	3 (1.8%)	6 (3.6%)	8 (4.8%)	0	5 (3.0%)	51 (30.7%)
55-64	5 (3.0%)	6 (3.6%)	3 (1.8%)	1 (0.6%)	9 (5.4%)	1 (0.6%)	4 (2.4%)	29 (17.5%)
65-74	8 (4.8%)	3 (1.8%)	4 (2.4%)	2 (1.2%)	3 (1.8%)	0	4 (2.4%)	24 (14.5%)
>75	7 (4.2%)	0	1 (0.6%)	0	0	0	0	8 (4.8%)
Total	52 (31.3%)	20 (12.0%)	14 (8.4%)	16 (9.6%)	46 (27.7%)	2 (1.2%)	16 (9.6%)	166 (100%)

The table presents the distribution of breast cancer subtypes across different age groups, based on a total of 166 cases. The most common subtype is Luminal A (52 (31.3%)), followed by Triple-Negative Breast Cancer (TNBC) (46 (27.7%)). Luminal B HER2-negative (20 (12.0%)) and HER2-enriched (16 (9.6%)) subtypes are also notable. A smaller proportion falls under the ER-negative, PR-positive category (2 (1.2%)), while cases where testing couldn't be done account for (16 (9.6%)). The highest number of cases is observed in the 45-54 years age group (51 (30.7%)), whereas the youngest age group (<25 years) has very few cases (5 (3.0%)). The majority of cases are seen in middle-aged and older individuals. (Table 3)The most commonly used chemotherapy regimen was AC 2-weekly followed by 2-weekly paclitaxel, administered to 49 (29.5%) patients. TAC was also widely used, given to 29 (17.5%) patients. (Table 4)

Table 4 : Chemotherapy Regimens for Breast Cancer Patients (n=166)

Regimen	n (%)
AC 2-weekly followed by weekly paclitaxel[1]	30 (18.1%)
AC 2-weekly followed by 3-weekly docetaxel[2]	17 (10.2%)
EC followed by weekly paclitaxel[3]	3 (1.8%)
EC followed by 3-weekly docetaxel[3]	6 (3.6%)
AC 2-weekly followed by 3-weekly paclitaxel[1]	22 (13.3%)
AC 2-weekly followed by 2-weekly paclitaxel[1]	49 (29.5%)
TAC[4]	29 (17.5%)
Hormonal agent	9 (5.4%)
EC followed by 2-weekly paclitaxel[3]	1 (0.6%)

[1]AC: Adriamycin (doxorubicin) + Cyclophosphamide, [2] Docetaxel-based regimen, [3] EC: Epirubicin + Cyclophosphamide, [4] TAC: Docetaxel + Adriamycin (doxorubicin) + Cyclophosphamide

Discussion

A cross-sectional study was conducted at the Department of Medical Oncology at Sushil Koirala Prakhar Cancer Hospital (SKPCH), Khajura Banke, over a period of six years from 2018 to January 2024 to assess the pattern of breast cancer in the western region of Nepal.

Among the various risk factors for breast cancer, female gender is a significant one, with the majority of reported cases being female (98.8%). The female-to-male ratio was 82:1. This finding supports the notion that breast cancer in males, though rare, cannot be neglected as it accounts for approximately 1 in 100 cases.[15]

The age of the patient is an important factor influencing the clinical prognosis of breast cancer, as multiple studies have shown that younger age at presentation carries a higher risk of recurrence and aggressive disease. The most common presentation in our study was in the fourth decade of life, which is notably earlier than in Western populations. This aligns with findings from a meta-analysis that reported an earlier incidence of breast cancer among Asian populations compared to Western populations.[13]

Although breast cancer is more common among postmenopausal women who are obese, our findings contradict Western data, as most of our cases (70, 42.2%) had a normal BMI (17.5 to 22.99). This difference may be attributed to lifestyle variations, socioeconomic factors, dietary habits (such as red meat and pork consumption), smoking, alcohol intake, and the earlier age of breast cancer presentation in Asian populations.

The usage of tobacco (via smoking or chewing) has been demonstrated to be causally linked to the development of several types of cancer. In the case of breast cancer, it has been found that tobacco consumption increases the risk of developing hormone receptor-positive breast cancer.[16] In our study, 42 (25.3%) patients had a history of tobacco consumption, either in smoked or chewed form. These findings contrast with Jones, M.E. et al. (2017), who also concluded that smoking was linked to a small but significantly higher risk of breast cancer, especially among women who started smoking during adolescence or around their first menstrual period.[17]

Alcohol is categorized as a Group 1 human carcinogen by the International Agency for Research on Cancer, contributing to 7 out of every 100 new breast cancer cases.[18] In our study, 28 (16.9%) patients had a history of alcohol intake in any amount. Given that Asian populations generally

have lower BMI than Western populations, it has been observed that the risk of breast cancer increases with alcohol consumption in women with BMI ≤ 25 kg/m² (RR = 1.03; 95% CI: 1.00–1.05 per 5 g/day rise), but not in women with BMI > 25 kg/m².[19]

A family history of breast cancer in a first-degree relative (mother, sister, or daughter) is associated with a two- to threefold increase in the risk of developing the disease. Up to 10% of breast cancers have been found to be hereditary.20 However, in our study, only a few patients had a family history of breast disease. The lower incidence of familial breast cancer in our study could be due to the small sample size and the predominance of elderly patients in our cohort.

Among 155 individuals, 54 experienced a delay of up to three months between the onset of symptoms and receiving treatment, while 101 patients (60.8%) experienced a delay of more than three months. The primary reasons for this delay were a lack of awareness regarding the severity of the disease and the absence of noticeable tumor symptoms. This underscores a significant gap in breast cancer awareness, screening, and early detection efforts.[21]

The left breast had the highest number of breast cancer cases (88), followed by the right breast (75). A few cases of bilateral breast cancer were also observed, affecting both breasts simultaneously. These findings align with previous studies.[14]

The presentation of breast cancer varies depending on the stage of the disease. In this study, the majority of cases presented with a lump in either the breast or axilla, consistent with findings from another study, *Clinical profile of patients presenting with breast cancer in Nepal*, where 98.2% of patients presented with a lump.[22] This suggests that the primary reason for seeking medical attention was the presence of a palpable mass rather than other symptoms.

Unlike Western countries with a high Human Development Index (HDI), where effective screening programs, health facilities, insurance coverage, and public awareness lead to early detection in 60–70% of cases (Stage I & II),[19] the scenario is different in low-development index (LDI) countries like Nepal and India. Here, the majority of cases present in locally advanced stages. In our study, Stage IIIA (55, 33.1%) was the most common, followed by Stage IIIB (39, 23.5%) and Stage IV (26, 15.7%). A similar trend was observed by Jha, A.K. et

al. (2010), who reported that over an eight-year period (1999–2008), more than 50% of breast cancer patients in Nepal presented in Stage III or IV.[23]

The majority of patients were estrogen receptor (ER) positive (95 vs. 65), i.e., 57.2% vs. 39.2%, while progesterone receptor (PR) positivity was observed in 78 vs. 82 (47.0%). Similar hormone receptor positivity rates of 50–60% have been reported in Indian populations, which is lower than in Western populations. This similarity may be due to shared epidemiological factors between India and Nepal.[24]

Approximately 20–30% of breast cancer tumors exhibit overexpression of Human Epidermal Growth Factor Receptor 2 (HER2), which is associated with more aggressive disease, higher recurrence rates, and increased mortality. HER2 receptor amplification was found in 32 patients (19.3%), while 118 (71.7%) cases were HER2-negative. Our findings are comparable to Indian data, where similar HER2 prevalence rates have been reported.[25,26] Several factors may contribute to the higher prevalence of triple-negative breast cancer (TNBC) in our population, including early age of onset, lifestyle factors (diet and obesity), reproductive history (multiparity), socioeconomic status, and screening behavior.

It has been established that breast cancer in younger and older age groups differs in molecular subtypes and prognosis. The most prevalent molecular subtype in our study was Luminal A (52, 31.3%), followed by TNBC (46, 27.7%) and Luminal B HER2-negative (20, 12.0%) and HER2-positive (14, 8.4%). Luminal A is the most common molecular subtype of breast cancer worldwide, accounting for 50–60% of cases, which supports our findings. However, in many Indian and Asian studies, TNBC is observed more frequently than in Western populations. In our study, 27.1% of patients had TNBC, which aligns with findings by Arpita et al., who reported a 40% prevalence of TNBC.[25]

It has been proven that the breast cancer in young and older age have different molecular subtype and prognosis. Most prevalent molecular subtype in our study was Luminal A 52 (31.3%) followed by Triple negative 46 (27.7%), luminal type B {her 2 +ve 20(12.0%) ; 14 (8.4%). Luminal type A is the most common molecular subtype in breast cancer worldwide and it accounts for the 50-60% of the breast cancer cases which justifies our finding. However, it has been observed

in many Indian and Asian continent that the triple negative breast cancer is much common then the western people in our study the 27.1% of the patient were triple negative (TN) the finding is quite concordant with finding in Arpita et.al where they as well observed the 40% of the TNBC [19] This suggests disparities in molecular subtypes and prognosis between Western and Asian populations. TNBC is particularly common among younger patients (<45 years), with incidence progressively decreasing with age.

Conclusion:

Breast cancer is the top most common cancer in the women in Nepal and it is the 4th most common cause of cancer related death. the holocaust of the breast cancer is increasing. Our study find that the breast cancer peaks around 4th to 5th decade. Luminal type A is most common followed by Triple negative breast cancer. The lack of adequate health insurance coverage, difficult geographical terrain, lack of awareness has led to delayed presentation in the breast cancer at advance stage III and IV.

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