

Original Article**EPIDEMIOLOGICAL AND MOLECULAR CHARACTERIZATION OF BREAST CANCER PATIENTS: A RETROSPECTIVE STUDY AT A NEPALESE TERTIARY CARE HOSPITAL*****Kushal Rizal¹, Birendra Kumar Yadav², Rajit Rattan¹, Alok Thakur², Mukti Devkota³, Ujwal Rai⁴**¹Department of Medical Oncology, ²Department of Radiation Oncology, ³Department of Surgical Oncology, ⁴Department of Pathology, Purbanchal Cancer Hospital, Birtamode, Jhapa, Nepal**Submitted: 27th-March-2025 Revised: 10th-May-2025 Accepted: 19th-May-2025****ABSTRACT****Background**

Breast cancer is a significant health burden in Nepal, ranking among the most common cancers in women, with increasing incidence in younger populations and limited comprehensive data. This study addresses the gap in understanding its clinical and demographic profile in a resource-limited setting. To characterize the demographic, clinical, pathological, and treatment profiles of breast cancer patients at a tertiary cancer hospital in Nepal from 2020 to 2023.

Methods

A retrospective analysis was conducted using data from the Health Management Information System for 404 breast cancer patients diagnosed at a tertiary cancer hospital. Patients with non-breast cancer diagnoses (n=2360) were excluded. Data included age, smoking/drinking habits, comorbidities, BMI, tumor laterality, TNM stage, molecular subtypes (ER/PR, HER2 status), and treatment modalities. Univariate analysis described patient characteristics, while bivariate analysis explored associations between age and molecular subtypes. Analysis was performed using STATA.

Results

Of 404 patients, 47.5% were aged 45–59 years, 26.5% ≥ 60 years, and 26% <45 years. Most (52.7%) did not smoke/drink, 33.2% had comorbidities, and 41.6% were overweight/obese. Breast cancer was nearly equally distributed between left (43.3%) and right (44.3%) breasts, with 31.9% at stage III and 10.6% at stage IV. Among 239 patients with immunochemical data, 38.1% were ER/PR+ and HER2-, and 27.6% had triple-negative breast cancer (TNBC), prevalent in the 45–59 age group (59.1%). Treatments included surgery (55.9%, predominantly modified radical mastectomy), chemotherapy (60.6%), radiotherapy (48.0%), hormonal therapy (32.9%), and immunotherapy (5.4%). Hormonal therapy was common in ER/PR+ and HER2- patients.

Conclusion

This study highlights a high prevalence of advanced-stage breast cancer and TNBC, particularly in middle-aged women, with a multimodal treatment approach. The findings underscore the need for early detection, comprehensive registries, and targeted therapies to address Nepal's growing breast cancer burden.

Keywords: Breast Cancer, Epidemiology, Molecular Subtypes, Nepal, Retrospective Studies, Triple-Negative Breast Cancer



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INTRODUCTION

Breast cancer is the most prevalent cancer globally and a primary cause of cancer-related mortality in women.¹ In 2020, 2.3 million women received a breast cancer diagnosis, resulting in 685,000 global fatalities.² These figures obscure significant disparities in prevalence across different geographies. The age-standardized incidence rate is 75.7 per 100,000 females in countries with a high Human Development Index (HDI), compared to 36.1 per 100,000 in regions with low HDI.³ However, the incidence rates are increasing rapidly in low and medium HDI countries. Three to five Additionally, due to the substantial population size, the incidence of breast cancer is significantly greater in low and medium Human Development Index (HDI) countries and is expected to rise further with increasing life expectancy.

Cancer constitutes 9% of total annual mortality and ranks as the third leading cause of death from non-communicable diseases in Nepal. According to GLOBOCAN estimates, Nepal recorded 20,508 new cancer cases and 13,629 cancer-related deaths in 2020, with breast cancer ranking as the fourth leading cause of cancer mortality.⁶ In 2022, the age-standardized incidence and mortality rates of breast cancer in Nepal were 14.4 per 100,000 and 7.6 per 100,000, respectively, which are comparatively low relative to other countries in the South Asia region. Seven Breast cancer represents a major health concern in Nepal, ranking among the most prevalent cancers in women. Research shows a rising incidence of breast cancer among younger demographics, resulting in more aggressive disease manifestations.⁸

In Nepal, significant risk factors for breast cancer encompass tobacco use (both smoking and smokeless), betel quid, areca nut, air pollution (indoor and outdoor), alcohol consumption, and viral infections such as Hepatitis B, Hepatitis C, HIV, and Human Papilloma Virus, as well as *Helicobacter pylori* and various dietary practices.⁹ Hereditary and genetic factors, including a first-degree relative with cancer and mutations in the BRCA1 and BRCA2 genes, contribute to 5% to 10% of cases of breast carcinoma.^{10,11} Risk factors may be classified into reproductive and non-reproductive categories. Reproductive risk factors encompass early onset of menstruation (prior to age 12), late onset of menopause (beyond age 55), nulliparity (never having given birth), advanced age at first full-term pregnancy (after age 30), and the absence of breastfeeding.¹² Obesity and a sedentary lifestyle are significant non-reproductive factors.^{13,14,15}

It is important to recognize that breast cancer management exhibits immunological heterogeneity and necessitates a multidisciplinary approach to treatment. Four molecular subtypes are identifiable based on the expression of estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth

factor receptor 2 (HER2).¹⁶ Each molecular subtype exhibits distinct risk factors, rates of progression, and prognostic outcomes.¹⁷ Luminal A breast cancers, characterized by positivity for estrogen receptor (ER) and/or progesterone receptor (PR), represent the most common subtypes and are associated with favorable prognoses. Triple negative breast cancer is characterized by the absence of estrogen receptor (ER) and progesterone receptor (PR) expression, as well as the lack of HER2 overexpression. Triple negative cancers exhibit aggressive behavior and are associated with a poor prognosis. Luminal breast cancers exhibit greater sensitivity to hormonal therapies, whereas triple-negative breast cancers demonstrate increased responsiveness to chemotherapy.¹⁷ Therefore, profiling clinical presentations and risk factors is crucial for a comprehensive understanding of disease burden and management strategies.

While Breast cancer is progressively becoming a growing burden, the disease has not been profiled extensively in over a decade in Nepal. There is limited evidence which is fragmented and the absence of comprehensive cancer registry highlights significant gaps in our understanding of the disease.¹⁸⁻²² This retrospective study was conducted to analyze the profile of breast cancer patients at a tertiary care center in Nepal. This study aims to present a detailed clinical and demographic profile of breast cancer patients at a tertiary cancer hospital in Nepal.

METHODS

This retrospective study analyzes data from patients diagnosed with breast cancer at a tertiary Cancer Hospital in Nepal between 2020 and 2023, a facility serving as a hub for specialized cancer care. The study received approval from the hospital administration to access de-identified patient data extracted from the Health Management Information System (HMIS). As such, no additional ethics approval or informed consent was required, in alignment with the Declaration of Helsinki and Good Clinical Practice Guidelines.

Data for 404 breast cancer patients were extracted from the hospital's Health Management Information System (HMIS), with the exclusion of 2,360 non-breast cancer cases (Figure 1). The clinical Tumor Node Metastasis (TNM) system was employed to evaluate cancer staging, focusing on tumor dimensions, involvement of regional lymph nodes, and presence of distant metastasis. Demographic and behavioral characteristics, such as age, smoking and drinking habits, comorbidities, and BMI, were sourced from the HMIS. Age was classified into three categories: less than 45 years, 45 to 60 years, and 60 years or older. Smoking and drinking habits, as well as comorbidities, were recorded as either "Yes" or "No." Body Mass Index (BMI) was categorized as under-

weight (less than 18.5), normal (18.5 to 22.9), overweight (23 to 29.9), or obese (greater than 30). Laterality was categorized as right, left, or undefined. Immunohistochemical testing assessed estrogen receptor/progesterone receptor (ER/PR) and HER2/neu status, classified as ER/PR+ and HER2-, ER/PR+ and HER2+, ER/PR- and HER2+, triple negative, ER/PR+, or other categories (including ER/PR negative, HER2 positive; ER/PR/HER2 not performed; or ER/PR+, HER2 equivocal). Treatment modalities were classified into surgery, radiotherapy, chemotherapy, targeted therapy, immunotherapy (Trastuzumab), and hormonal therapy.

Univariate analysis described patient characteristics, histological types, cancer stage, molecular profile, and treatment types, while bivariate analysis explored associations between age and molecular type. No formal sample size calculation was performed, as all available breast cancer cases in the HMIS were included. Analyses were conducted using STATA software. Figure 1 illustrates the patient flow diagram.

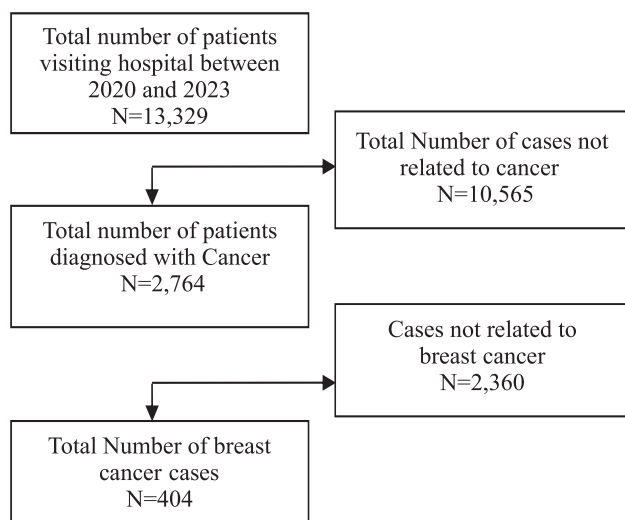


Figure 1: Patient Flow Diagram

RESULTS

Number of Patients

Between 2020 and 2023, 2764 patients were diagnosed with cancer at the facility (Figure 1). The information for the patients were extracted from the HMIS of the hospital. The analysis is based on data for 404 patients who were diagnosed with breast cancer.

Profile of Patients

Among 404 patients, 107 (26.5%) were aged over 60 years, while 192 (47.5%) were in the age group 45 to 59 years (Table-1). A higher portion of the patients did not smoke/drink (52.7%), and 14 (3.5%) either smoked/consumed tobacco. 134 patients (33.2%) reported comorbidities, 39 patients (9.7%) were obese and 129 (31.9%) were overweight.

Table 1: Summary characteristics of the patients

Age	N	%
Less than 45 years	105	26
45 to 59 years	192	47.5
60 years and above	107	26.5
Habit (Smoke/drink)		
No	213	52.7
Yes	14	3.5
Missing	177	43.8
Comorbidities		
No	245	60.6
Yes	134	33.2
Missing	25	6.2
Body Mass Index category according to Asian Standard		
Less than 18.5	13	3.2
18.5-22.9	54	13.4
23-29.9	129	31.9
>=30.0	39	9.7
Missing	169	41.8
Total	404	100

Pathological type and TNM stage of the Patients

Of the 404 patients, 179 (44.3%) had cancer in right breast and 175 (43.3%) in left breast (Table-2). When examining the stage of cancer, most patients were at an advanced stage, with 43 patients (10.6%) in Stage IV and 129 patients (31.9%) in Stage III (Table-2). Only a small percentage (5%) were in the Stage I. While 27.2% (110) of the patients were in stage 2.

Table 2: Pathological type and TNM stage of the Patients

	N	%
Laterality		
Left	175	43.3
Right	179	44.3
Not defined	50	12.4
Stage		
1	20	5
2	110	27.2
3	129	31.9
4	43	10.6
Not Staged	102	25.2
Total	404	100

Clinical characteristics of the Patients

Immunochemical testing results were obtained for 239 patients (Table-3). Triple negative breast cancer (TNBC) was identified in 27.6% (66) of the 239 patients studied. Of the patients, 38.1% were positive for ER/PR and negative for HER2/neu.

Table 3: Hormone profile of the Patients

	N	%
ER/PR + and HER2/neu -	91	38.1
ER/PR + and HER2/neu +	32	13.4
ER/PR - and HER2/neu +	27	11.3
Triple negative	66	27.6
ER/PR +	9	3.8
Others	14	5.9
Total	239	100

A total of 226 cases underwent surgery, representing 55.9% of the sample (Table-4). Among these surgical procedures, the most common surgery performed was Modified Radical Mastectomy (MRM), accounting for 75.7%, 171 cases of all surgeries (Table-4). Radiotherapy was utilized in 48.0%, 194 cases of the sample and Chemotherapy was administered in 60.6%, 245 cases of instances (Table-4). Immunotherapy, specifically Trastuzumab, was administered in 5.4%, 22 cases of patients. Hormonal therapy was employed in 32.9%, 133 cases of the cases.

Table 4: Treatment received by the Patients

	N=404	%
Surgery	226	55.9
MRM	171	75.7
MRM + ALND/DIEP/SNLB	24	10.6
Lumpectomy/BCS	15	6.6
BCS + SNB/ALND/Hemithyroidectomy	4	1.8
WLE + SLNB/ALND	3	1.3
Others	9	4
Radiotherapy	194	48.0
Chemotherapy	245	60.6
Target therapy	4	1.0
Lapatinib	1	25
Palbociclib	3	75
Immunotherapy (Tarastuzumab)	22	5.4
Hormonal therapy	133	32.9
Anastrozole	4	3
Letrozole	60	45.1
Tamoxifen	55	41.4
Anastrozole, Tamoxifen	3	2.3
Letrozole, Tamoxifen	10	7.5
Letrozole, Anastrozole	1	0.8

Triple negative breast cancer is observed in 59.1% of patients within the 45-to-59-year age group, as indicated in Table 5. The prevalence of ER/PR positive and HER2/neu negative is noted. The prevalence of ER/PR and HER2/neu positivity is significantly higher in patients over 60 years of age (Table 5).

Table 5: Distribution of molecular subtypes by age

	N=91 ER/PR + and HER2/neu -	N=32 ER/PR + and HER2/neu +	N=27 ER/PR - and HER2/neu +	N=66 Triple negative	N=9 ER/PR +	N=14 Others
Less than 45 years	28.6	40.6	33.3	27.3	33.3	14.3
45 to 59 years	40.7	40.6	40.7	59.1	33.3	71.4
60 years and above	30.8	18.8	25.9	13.6	33.3	14.3
Total	100	100	100	100	100	100

Majority of patients across all molecular subtypes underwent surgery, radiotherapy, and chemotherapy. Among those who received hormonal therapy, a high proportion of patients were ER/PR + and HER2/neu – (62.7%) (Table-6). Immunotherapy with Trastuzumab, primarily indicated for HER2-positive breast cancer, was administered to 17 patients (Table-6). Relatively a high number of patients with triple negative cancer received chemotherapy.

Table 6: Distribution of molecular subtypes by treatment received by the patients

	ER/PR + and HER2 /neu -	ER/PR + and HER2 /neu +	ER/PR and HER2 /neu +	Triple negative	ER/PR +	Others	Total
Surgery	N 58 % 36.9	24 15.3	19 12.1	45 28.7	3 1.9	8 5.1	157 100
Radiotherapy	N 58 % 38.9	18 12.1	20 13.4	46 30.9	1 0.7	6 4	149 100
Chemotherapy	N 68 % 40.7	16 9.6	20 12	54 32.3	1 0.6	8 4.8	167 100
Target therapy	N 2 % 66.7	0 0	0 0	0 0	0 0	1 33.3	3 100
Immunotherapy (Tarastuzumab)	N 0 % 0	8 40	9 45	2 10	0 0	1 5	20 100
Hormonal therapy	N 64 % 62.7	25 24.5	0 0	4 3.9	7 6.9	2 2	102 100

DISCUSSION

The study provides insights into the histological characteristics, demographics, molecular profile and risk factors of breast cancer patients in the study population. Following are the salient findings from this study.

Approximately 50% of patients were aged between 45 to 59 years, while a quarter of patients were aged over 60 years. This suggests that breast cancer affects individuals across various age ranges, with a significant representation in middle-aged and older populations. Earlier studies for Nepal based on hospital level data have also found that more than 70% of patients were above 40 years.^{18,22} A recent study on breast cancer shows a rise in cases among females under 50 from 1990 to 2017 across most of the regions except North America and Europe and Central Asia.²³ This

increase is more significant in those who are <50 years as compared to those over 50 years. Additionally, mortality rates have consistently risen in both age groups in South Asia.

One third of patients reported comorbidities, while the majority did not have any reported comorbid conditions. Additionally, a significant number of patients were overweight or obese. A retrospective study conducted at a tertiary facility in Nepal in 2006 to identify the risk factors found that 20% of women in the sample were obese.¹¹ It is expected that with changing lifestyle the prevalence of obesity is likely to increase. These findings underscore the potential impact of comorbidities and obesity on breast cancer incidence and prognosis. Here it is worth noting that several studies have shown that being overweight or obese, especially after menopause, can elevate the risk of developing breast cancer.^{24,25} This association is thought to be due to the higher levels of estrogen produced by fat tissue after menopause, which can promote the growth of hormone receptor-positive breast cancers. Further, obese people are more likely to suffer from co-morbidities which is likely to complicate the treatment of breast cancer.

Breast cancer distribution showed a nearly equal occurrence in the right and left breasts. However, it is known that occurrence in the left breast is quite common and have poor survival.²⁶ Further, more than one third of the patients presented with advanced-stage cancer which could lead to a poor survival outcome. Earlier studies for Nepal have also found that most of the patients are more likely to be diagnosed at an advanced stage.^{18,20,21} These findings emphasize that no significant improvement has taken place in early detection and intervention to improve breast cancer outcomes are required. In fact, a recent systematic review found that screening for breast and cervical is particularly low for South Asian emigrants due to poor knowledge about cancer and socio-cultural practices.²⁷ The problem is compounded by shortage of health care workers and necessary infrastructure.⁹ Towards this end recently a lot of countries have found iBreastExam as an important low-cost tool to screen for breast cancer in low resource setting.²⁸

In a cohort of patients with accessible immunochemical testing results, over 25% received a diagnosis of triple-negative breast cancer (TNBC). A significant proportion (38.1%) of patients demonstrated estrogen receptor (ER)/progesterone receptor (PR)-positive and HER2/neu-negative status, highlighting the heterogeneity of breast cancer molecular profiles in the study population. The findings align with a recent study indicating that 25% of patients experienced triple negative cancer.¹⁸ Additionally, our findings indicate that triple negative breast cancer is common among a significant proportion of patients aged 45 to

59 years. Luminal breast cancers exhibit greater responsiveness to hormonal therapies, whereas triple-negative breast cancers present limited treatment alternatives.¹⁷ Triple negative cancers exhibit increased aggressiveness, a higher likelihood of recurrence, and lower survival rates. The findings indicate a need for additional clinical research focused on targeted therapies and immunotherapies to enhance survival outcomes for this cancer subtype.

Surgical intervention was the most common treatment approach, with 55.9% of patients undergoing surgery. Modified Radical Mastectomy (MRM) was the predominant surgical procedure, performed in 75.7% of cases. Additionally, radiotherapy (48.0%), chemotherapy (60.6%), hormonal therapy (32.9%), and immunotherapy (5.4%) were utilized in varying proportions. These findings reflect the multimodal nature of breast cancer treatment, with a combination of surgery, systemic therapy, and targeted interventions employed to optimize patient outcomes. In our study, the use of hormonal therapy to treat a high proportion of patients who are ER/PR + and HER2/neu – reflects a move towards personalized approach.

This study has some caveats. There were challenges in obtaining complete information for certain important indicators as the study followed a retrospective design. For example, the information on histological type of breast cancer was not available and information on BMI, stage of cancer and smoking habit was missing for many patients.

Additionally, the dataset lacked information on several known risk factors, such as lack of exercise, sedentary lifestyle, breast density, family history, nulliparity, delayed childbirth and high fat diet. This absence of data prevents us from gaining insights about the behaviour and habits of the patients. However, having additional data related to these missing variables would have been beneficial in gaining a more nuanced understanding of the factors contributing to breast cancer in this population.

This study may not fully represent the diversity of breast cancer patients across different geographic regions or healthcare settings. This could limit the generalizability of the results to broader populations and could induce a selection bias. Further, the size of the sample also did not permit the use of statistical tests following the bivariate analysis. However, we have tried to present the distribution of hormonal profile by age and type of treatment.

CONCLUSION

In summary, our study provides comprehensive insights into the demographic profile, clinical characteristics, and treatment patterns of breast cancer patients. The findings underscore the complex interplay of factors influencing breast cancer risk and management, including age, lifestyle habits, comorbi-

dities, and molecular profile. While surgical intervention remains a cornerstone of treatment, the utilization of adjuvant therapies reflects a move towards personalized approach tailored to subtype and disease stage. Strategies to enhance breast cancer outcomes rely on essential health system strengthening to provide effective treatments that are already established. Moving forward, continued research efforts aimed at explaining the molecular underpinnings of breast cancer and refining therapeutic approaches are crucial for advancing breast cancer care and reducing disease burden.

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