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Original Research Article

Retrospective analysis of breast cancer subtypes, risk factors, and lump features: outcomes from a tertiary care hospital in Multan, Pakistan

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ABSTRACT

Background: Breast cancer is the most frequently diagnosed malignancy and a leading cause of cancer-related mortality among Pakistani women. Despite its high prevalence, patients in Pakistan are often diagnosed at advanced stages, resulting in poor prognosis. This study aimed to assess the frequency of different breast cancer subtypes, clinical features, staging, grading, and receptor statuses among patients in southern Punjab.
Methods: A retrospective analysis was conducted at Nishtar Cancer Center, Multan, from October 2024 to February 2025, using medical records of 193 female patients diagnosed with breast tumors in 2024. Demographic details, risk factors, tumor characteristics, and receptor status were analyzed using statistical package for the social sciences (SPSS) version 26.0.
Results: Most patients (47.2%) were aged 40–60 years, with 96.9% being married and 17.6% having a history of breastfeeding. Most tumors were invasive ductal carcinoma (90.7%), commonly located in the upper outer quadrant (69.4%). Advanced-stage disease was prevalent, with T4 tumors (38.3%) and N1 lymph node involvement (43.5%). Grade III tumors were frequent (60.1%), and receptor analysis showed luminal B (31.6%) as the most common subtype, followed by luminal A (30.1%) and triple-negative (25.4%).
Conclusions: The findings highlight the late-stage diagnosis and aggressive nature of breast cancer in this region, emphasizing the urgent need for enhanced awareness, early screening programs, and improved healthcare accessibility to facilitate early detection and better treatment outcomes.

Keywords: Breast cancer, Retrospective study, Risk factors, Pakistan

INTRODUCTION

Breast cancer is a malignant growth that originates in ducts or glandular tissue of the breast. It affects women globally, contributing to alarmingly high mortality rates. The World Health Organization (WHO) estimates that around 1.2 million people are diagnosed with breast cancer every year. In rare cases, it can also occur in males. In Pakistan, breast cancer stands as the leading cause of cancer-related fatalities among women, as confirmed by comprehensive research.[1] Furthermore, it is the most commonly diagnosed cancer in the country. For instance, one in every nine Pakistani women suffers from breast cancer, highlighting the urgent need for awareness and proactive measures. The prevalence of breast cancer in Pakistan is 2.5 times higher compared to its neighboring countries like Iran and India. As specified by data from Shaukat Khanum Memorial Cancer Hospital, the incidence of breast cancer is 45.9% among female patients and 21.5% among all patients.[2]

Pakistani women are diagnosed with breast cancer at later stages. When initially diagnosed, the tumors are usually

large and have often spread to the axillary lymph nodes. For breast cancer detected at stages 1 and 2, the survival rate is 85%; however, for late-stage diagnosis, notably stage 4, it significantly drops to 10%. Thus, early detection and treatment play a pivotal role in the management and treatment of breast cancer. For this purpose, several screening methods have been established including breast self-examination, clinical breast examination, and mammography.[3]

The factors contributing to the risk of developing breast cancer are numerous and complex. They include aging, genetic mutations, previous exposure to radiation therapy, a family history of breast cancer, a personal history of breast cancer or specific benign breast disease, use of hormonal treatment especially menopausal or oral contraceptives, postmenopausal weight gain or obesity, menopause occurring after the age of 55, nulliparity, late age at first full-term pregnancy, old age at first live birth or fewer pregnancies, shorter duration of breastfeeding or no breastfeeding at all, early menarche, presence of increased breast density, sedentary lifestyle, history of smoking and alcohol intake, change of dietary patterns and exposure to environmental toxins like organochlorine pesticides.[4-6]

Breast cancers are classified into various forms based on their grading, staging, receptor stages, and histological markers, which is essential when deciding treatment approaches.[7] Grading compares healthy breast tissue to normal breast tissue. Normal cells adopt distinct shapes, while cancerous cells lose this differentiation.

Breast cancer staging is carried out via the tumor, node, metastasis, (TNM) system. This classification system assesses the tumor size (T), determines whether the cancer has spread to the lymph nodes (N) in the axillary region, and indicates the presence of metastasis. The staging is categorized as stage 0 representing pre-cancerous or marker condition, and stage 1-3 reflecting the extent of the cancer within the breast or its involvement within the nearby lymph nodes. Stage 4 indicates metastatic cancer, which generally carries an adverse prognosis.[8]

Certain receptors, including progesterone (PR), estrogen (ER), and HER2 are found in breast cancer cells, which give rise to molecular and intrinsic subtypes. Intrinsic subtypes include luminal type A (ER+/ HER-), which has the most favorable prognosis, luminal type B (ER+/HER+), HER2-enriched (HER2+/ER-/PR-), and triple-negative/basal-like subtype which has less favorable prognoses as compared to other subtypes.[8-10] Histological analysis classifies tumors into the following groups; A (invasive ductal carcinomas), B (tubular, papillary carcinomas), C (metaplastic, anaplastic carcinomas), D (invasive lobular carcinomas), E (mixed ductal carcinomas), and unknown (unable to be classified).[11]

One of the most common presenting symptoms of breast cancer in females is a lump or swelling in the breast.[12] The predominant lesions that lump in the breast include fibroadenoma, fibroadenosis, and carcinoma.[13] The upper outer quadrant is the most commonly involved location for lumps in females. Other symptoms include breast pain, tightness and tingling in the breast, swollen breasts, enlarged breasts with redness, ulcers over the breast, inverted nipple, nipple discharge, anorexia, and weight loss.[14] The objective of this research was to calculate the frequency of different breast cancer subtypes and clinical features of breast lumps. Furthermore, it aims to analyze the stages, grades, receptor statuses, and ultrasonic characteristics of various breast cancer types in southern Punjab.

METHODS

Study design

A retrospective analysis was conducted from October 2024 to February 2025 at Nishtar Cancer Center, Multan, Pakistan. The study utilized secondary data extracted from the medical records of patients treated throughout the year 2024. Ethical approval was obtained from the Institutional Review Board of Nishtar Medical University. Since the study relied on anonymized data from medical records and no patient-identifiable information was published, informed consent was not required.

The study included all female patients diagnosed with breast tumors (both benign and malignant) who were receiving treatment at Nishtar Cancer Center during the specified period. Patients with incomplete medical records were excluded from the study. A total sampling method was employed, encompassing all patients who met the eligibility criteria, resulting in a final sample of 193 subjects.

The data extracted from the medical records included demographic details such as the patient's name, age, marital status, and history of breastfeeding. Additionally, information regarding the patient's treatment history—including radiotherapy, and hormonal therapy—was recorded. The study also collected information on the patient's family history of malignancies, clinical features of the breast lump (such as size, site, and number), mammographic findings, and details regarding the diagnosis of the breast tumor, including staging, grading, and receptor status.

Statistical analysis

Descriptive analysis was performed with statistical package for the social sciences (SPSS) version 26.0. Data were presented in frequency and percentage.

RESULTS

A total of 193 subjects were recruited for the study. The study's demographic and breastfeeding data (Table 1) indicate that most participants were between 40 and 60

years old (47.2%), with a smaller proportion above 60 (19.7%). A vast majority (96.9%) were married, and 17.6% had a history of breastfeeding. These findings highlight the prevalence of breastfeeding among participants and suggest a primarily middle-aged population.

Table 1: Demographic and breastfeeding data.

Characteristics	Frequency (%)
Age (years)	
20-40	64 (34.2)
40-60	91 (47.2)
Above 60	38 (19.7)
Marital status	
Married	187 (96.95)
Unmarried	6 (3.1)
History of breastfeeding	
Negative	159 (82.4)
Positive	34 (17.6)

Table 2: Risk factors for breast cancer.

Risk factors	Frequency (%)
History of radiotherapy	
Exposed	6 (3.1)
Not Exposed	187 (96.9)
History of hormonal therapy	
Positive	1 (0.5)
Negative	192 (99.5)
History of breast disease	
Positive	20 (10.4)
Negative	173 (89.6)
Family history of any malignancy	
Positive	24 (12.4)
Negative	169 (87.6)

Lump clinical and mammographic findings present in Table 3 revealed that most breast lumps were located in the upper outer quadrant (69.4%), with a single lump being the most common presentation (84.5%). Nearly equal involvement of the right (47.2%) and left (51.3%) breasts was noted. Nipple retraction was observed in 15.5% of cases, while lymph node involvement was present in 64.8%. The dominant mammographic feature was a hypoechoic lesion with irregular margins (56.9%). Finally, Table 4 shows that invasive ductal carcinoma (90.7%) was the predominant cancer type, with the most common TNM classification being T4 (38.3%) and N1 (43.5%). Most patients (60.1%) had grade III tumors, and receptor status analysis revealed that luminal B (31.6%) was the most frequent subtype, followed closely by luminal A (30.1%) and triple-negative cases (25.4%).

Regarding breast cancer risk factors (Table 2), only 3.1% had a history of radiotherapy, and an even smaller fraction (0.5%) had undergone hormonal therapy. A history of breast disease was reported by 10.4% of individuals, while 12.4% had a family history of malignancy. These results suggest that common breast cancer risk factors were relatively infrequent in this population, which may indicate other contributing factors at play.

Table 3: Breast lump clinical features and mammographic findings.

Characteristics	Frequency (%)
Site of lump	
Upper outer quadrant	134 (69.4)
Upper inner quadrant	12 (6.2)
Lower outer quadrant	12 (6.2)
Lower inner quadrant	5 (2.6)
Central	30 (15.5)
Number of lumps	
One	163 (84.5)
Two	23 (11.9)
Three or more than three	7 (3.6)
Side of chest involved	
Right	91 (47.2)
Left	99 (51.3)
Both	3 (1.6)
Skin changes (erythema, ulceration, thickening)	
Present	99 (51.3)
Absent	94 (48.7)
Nipple retraction	
Retracted	30 (15.5)
Not retracted	163 (84.5)
Lymph nodes involvement	
Sentinel	115 (59.6)
Non sentinel	5 (2.6)
Both	5 (2.6)
Not involved	68 (35.2)
Mammographic features	
Dense parenchymal lesion	26 (13.5)
Hypoechoic lesion with irregular margin	109 (56.9)
Calcification	43 (22.3)

Table 4: Diagnosis and staging of breast cancer.

Characteristics	Frequency (%)
Diagnosis	
Invasive ductal carcinoma (IDC)	175 (90.7)
Invasive lobular carcinoma	12 (6.2)
Metaplastic carcinoma	2 (1)
Lobular carcinoma in situ (LCIS)	2 (1)

Continued.

Characteristics	Frequency (%)
Ductal carcinoma in situ (DCIS)	1 (0.5)
Fibroadenoma	1 (0.5)
TNM classification	
Values of T	
T1	19 (9.8)
T2	70 (36.3)
T3	30 (15.5)
T4	74 (38.3)
Value of N	
Nx	12 (6.2)
No	69 (35.8)
N1	84 (43.5)
N2	20 (10.4)
N3	8 (4.1)
Value of M	
Mx	17 (8.8)
Mo	144 (74.6)
M1	32 (16.6)
Grading	
I	2 (1)
II	74 (38.3)
III	116 (60.1)
IV	1 (0.5)
Receptor status	
Luminal A	58 (30.1)
Luminal B	61 (31.6)
HER2 enriched	25 (13)
Triple negative	49 (25.4)

DISCUSSION

According to global cancer statistics, Asia accounts for more than half of all cancer diagnoses (>19.3 million new cases) and approximately 10 million fatalities per year. The World Health Organization's (WHO) cancer statistics indicate that 47.8% of people have breast cancer.[15]

Our study results align with a previous retrospective analysis conducted at Aga Khan University and Hospital, Karachi, in 2016, which also found breast cancer to be most prevalent among females aged 40 to 60 years.[16] It can be due to prolonged exposure to reproductive hormones, particularly estrogen, over the years. Additional risk factors, such as delayed childbirth, fewer pregnancies, and the hormonal changes associated with menopause, further contribute to the increased likelihood of developing the disease during this stage of life. A significant portion of the study sample (82.4%) had no history of breastfeeding, highlighting the protective role that breastfeeding plays in reducing the risk of breast cancer. The hormonal changes that take place during lactation are thought to be responsible for this protective effect. These changes cause breast cells to differentiate and divide less frequently, which lowers the risk of genetic abnormalities that could cause cancer.[17]

In our study, the low prevalence of radiotherapy exposure (3.1%) stands out as a unique finding, highlighting a distinct aspect of our results suggesting it may not be a major contributing factor in this population. This is because multiple factors make radiotherapy a major concern. Radiation therapy-induced cancer is closely linked to a patient's age, with those receiving treatment before 30 years being at a higher risk of developing breast cancer while our group was mostly 40 to 60 years old. The choice of radiotherapy technique also plays a critical role in secondary cancer risk. For example, tangential field IMRT (2F-IMRT) carries a significantly lower risk compared to multiple-field IMRT (6F-IMRT) or double partial arcs (VMAT).[18] Another notable finding of our study is the relatively low occurrence of established breast cancer risk factors, such as a history of hormonal therapy (0.5%), breast disease (10.4%), and a family history of malignancy (12.4%). This could be influenced by factors like recall bias among participants, limited healthcare access, and potential genetic or environmental influences, making it an important aspect of our results.

Furthermore, the results showed that the breast lump was most commonly located in the upper outer quadrant (69.4%). This finding is consistent with most of the published studies in the literature, but the higher occurrence of breast cancer in the upper outer quadrant

remains unclear. One study attributes it to the greater amount of breast tissue in this area, while another suggests a disproportional increase, especially in younger women, possibly linked to cosmetic use near the underarm and upper breast.[19] Ultrasound or mammograms showed an irregular hypoechoic lesion in the maximum (56.9%) number of cases, which is a common finding, but malignant masses consisting of tumor cells mixed with tissues of varying echogenicity, including adipose tissue, fluids, hemosiderin, and microcalcifications, along with cellular heterogeneity, may contribute to hyperechogenicity on ultrasound also.[20]

Our findings highlight that the sentinel lymph node (SLN) was the most frequently involved (59.6%), whereas 35.2% showed no lymph node involvement. In principle, SLN is the first to receive lymph-borne metastatic cells, as it directly drains lymphatic fluid from the primary tumor, due to which Sentinel lymph node biopsy (SLNB) has become a standard procedure in breast cancer management, playing a key role in advancing less invasive surgical techniques.[21]

This study from Multan, Pakistan, reveals that invasive ductal carcinoma (IDC) is the predominant histological type, found in 90.7% of cases. Additionally, luminal B emerged as the most frequent molecular subtype, identified in 31.6% of patients, providing valuable insights into the breast cancer landscape in this region with results similar to another study by the College of Medicine, University of Duhok.[22]

However, luminal A is the most common type according to most published studies.[23] Compared to Oluogun et al, our study showed more advanced breast cancer at diagnosis, with higher T4 tumors (38.3% versus 4.3%), N1 lymph node involvement (43.5% versus 17.4%), and distant metastases (16.6% versus 4.3%).[24] Grade III tumors were also more frequent (60.1% versus 30.4%), highlighting a more aggressive disease pattern and the need for better early detection.

A key strength of our study is its comprehensive analysis of breast cancer subtypes, risk factors, and tumor characteristics in a tertiary care setting, contributing valuable regional data from Multan, Pakistan. The inclusion of a diverse patient population enhances the study's generalizability. However, limitations include the retrospective design, potential recall bias in medical records, and reliance on hospital-based data may not fully represent the general population.

CONCLUSION

The high proportion of advanced-stage and grade III tumors emphasizes the aggressive nature of breast cancer in this region and the need for improved early detection strategies. Strengthening breast cancer awareness, screening programs, and access to healthcare facilities is crucial for better patient outcomes in Pakistan.

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