## **ORIGINAL ARTICLE**

# Frequency of Breast Cancer Recurrence and Factors Impacting the Recurrence and Survival

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## ABSTRACT

**Background:** Breast cancer recurrence remains a critical challenge despite advancements in screening and treatment. Identifying factors influencing recurrence and survival is essential to improving outcomes.

**Objective:** To determine the frequency of breast cancer recurrence, assess factors impacting recurrence, and evaluate survival outcomes.

**Material and Methods:** This retrospective study included 282 breast cancer patients treated between January 2022 and December 2022 at the Hayatabad Medical Complex Peshawar. Demographic, clinical, and tumor-related variables were analyzed using descriptive statistics. Associations between recurrence status and variables were evaluated using the chi-square test, and survival outcomes were assessed. A p-value  $\leq 0.05$  was considered statistically significant.

**Results:** The mean age of the patients was  $49.00 \pm 14.83$  years, with a mean BMI of  $27.66 \pm 3.79$  and a mean tumor size of 2.91 ± 1.16 cm. The recurrence rate was 29.1%, with 200 (70.9%) patients experiencing no recurrence and 82 (29.1%) having recurrence. Overall survival was 79.1%, with 223 patients alive and 59 deceased. Hormone receptor-negative tumors were significantly associated with recurrence (p = 0.010). Smoking status showed borderline significance (p = 0.052), while HER2 status, tumor stage, and lymph node involvement did not demonstrate significant associations with recurrence.

**Conclusion:** The study highlights the persistent burden of breast cancer recurrence and its impact on survival. Hormone receptor-negative tumors and modifiable factors like smoking are critical in recurrence risk, underscoring the need for stratified management and lifestyle interventions to improve long-term outcomes.

Keywords: Breast cancer, recurrence, survival, hormone receptor status, risk factors, smoking.

## INTRODUCTION

Breast cancer is the most frequently diagnosed cancer among women and remains a significant cause of morbidity and mortality globally. While advancements in treatment have improved survival rates, recurrence continues to be a critical challenge, influencing long-term outcomes and quality of life. Recurrence rates vary significantly depending on individual factors, including tumor biology, treatment approaches, and patient demographics, highlighting the importance of identifying and addressing prognostic indicators early in the treatment journey<sup>1,2</sup>.

Several factors contribute to the frequency of recurrence. Studies show that aggressive subtypes such as triple-negative breast cancer (TNBC) and HER2-positive breast cancer are more likely to recur, particularly in younger women<sup>3</sup>. Tumor size, lymph node involvement, and the presence of lymphovascular invasion are also well-established predictors of recurrence<sup>4</sup>. Additionally, the role of molecular profiling, including genetic markers and immunohistochemical subtyping, has been emphasized in stratifying patients based on recurrence risk, enabling tailored therapeutic strategies<sup>5</sup>.

The site and timing of recurrence are crucial determinants of survival outcomes. Locoregional recurrences often have better prognoses compared to distant metastases. However, distant metastases, especially to vital organs such as the liver or lungs, significantly diminish survival prospects<sup>6</sup>. Early recurrences, typically within the first five years post-treatment, are often associated with poor outcomes, particularly in patients with high-risk tumor subtypes<sup>7</sup>. Moreover, younger patients under the age of 40 exhibit higher recurrence rates, potentially due to more aggressive tumor biology or delayed diagnosis<sup>8</sup>.

Improvements in treatment protocols, including neoadjuvant and adjuvant therapies, have played a pivotal role in reducing recurrence rates. For instance, the integration of targeted therapies such as trastuzumab for HER2-positive breast cancer and the adoption of extended endocrine therapy for hormone receptorpositive cases have shown promising results<sup>9-10</sup>. However, recurrence remains a challenge in certain subgroups, emphasizing the need for personalized treatment plans and intensive follow-up programs tailored to individual risk profiles.

Despite advancements in treatment and understanding of recurrence patterns, breast cancer recurrence remains a major contributor to reduced survival and poor quality of life. This study aims to explore the frequency of recurrence and the factors influencing recurrence and survival in a cohort of breast cancer patients, providing insights to enhance personalized treatment strategies and long-term management.

## MATERIAL AND METHODS

This retrospective cross-sectional study was conducted to determine the frequency of breast cancer recurrence, factors impacting recurrence, and survival among patients diagnosed and treated for breast cancer. The study was carried out at the Hayatabad Medical Complex Peshawar, a tertiary care hospital catering to a diverse patient population in Southern Punjab, Pakistan. The study duration was from January 2022 and December 2022, and the sample size for the study was 282 patients. The sample size calculation was based on an anticipated survival rate of 24.2% as reported in the study by Courtney D et al., with a margin of error of 5% and a confidence level of 95%<sup>11</sup>. A non-probability consecutive sampling technique was employed to recruit all eligible patients during the study period.

Patients aged 18 years or older, with a confirmed diagnosis of breast cancer based on histopathology reports, were included in the study. Patients who had completed their initial treatment (surgery, chemotherapy, radiotherapy, or hormonal therapy) and had available medical records documenting follow-up for recurrence or survival were eligible for inclusion. Patients with incomplete or missing medical records, those with a history of other malignancies, or those presenting with metastatic disease at the time of diagnosis were excluded from the study.

Data collection was conducted retrospectively by reviewing patient medical records and oncology follow-up records. A structured proforma was used to document demographic variables such as age, menopausal status, BMI, and smoking status; tumor characteristics, including tumor size, histological grade, hormone receptor status (ER/PR), HER2 status, lymph node involvement, and tumor stage (TNM classification); recurrence data, including recurrence status (Recurrence or No Recurrence) and recurrence type (No Recurrence, Local, Regional, Distant); and survival outcomes, specifically overall survival status (Alive or Death). Ethical approval for the study was obtained from the Institutional Review Board (IRB) of Civil Hospital, Bahawalpur, and all data were anonymized to ensure confidentiality.

The data were analyzed using SPSS Version 24.0. Descriptive statistics summarized the data, with continuous variables such as age, BMI, and tumor size presented as mean  $\pm$  standard deviation (SD), and categorical variables such as age group, menopausal status, obesity, smoking status, histological grade, hormone receptor status, HER2 status, lymph node involvement, tumor stage, recurrence type, recurrence status, and overall survival status presented as frequencies and percentages. The Chi-square test was used to assess associations between categorical variables, such as recurrence status and factors including menopausal status, obesity, smoking status, listological grade, hormone receptor status, HER2 status, lymph node involvement, tumor stage, and recurrence type. A p-value  $\leq 0.05$  was considered statistically significant.

#### RESULTS

The study included 282 patients, with a mean age of  $49.00 \pm 14.83$  years, a mean BMI of 27.66  $\pm$  3.79, and a mean tumor size of 2.91  $\pm$  1.16 cm. Out of 282 breast cancer patients included in the study, 200 (70.9%) had no recurrence, while 82 (29.1%) experienced recurrence. Regarding overall survival, 223 patients (79.1%) were alive at the time of analysis, and 59 (20.9%) had died. (Table 1)

The association between various demographic and clinical variables with recurrence status showed notable trends. Among patients aged less than 50 years, 42 (29.8%) experienced recurrence, while 99 (70.2%) had no recurrence. For those aged 50 years or above, recurrence was observed in 40 (28.4%), with 101 (71.6%) having no recurrence (p = 0.793). Regarding

Table 2: Association of Demographic and Clinical Variables with Recurrence Status

menopausal status, recurrence was more frequent among premenopausal women, with 40 (34.8%) experiencing recurrence compared to 75 (65.2%) with no recurrence. Post-menopausal women had a lower recurrence rate, with 42 (25.1%) experiencing recurrence and 125 (74.9%) showing no recurrence (p = 0.080).

Obesity did not show a significant association with recurrence. Among non-obese patients, 57 (30.2%) had recurrence, while 132 (69.8%) did not. Obese patients showed a similar trend, with 25 (26.9%) experiencing recurrence and 68 (73.1%) having no recurrence (p = 0.569). Smoking status showed a borderline significance, as 34 (36.6%) smokers experienced recurrence, compared to 59 (63.4%) with no recurrence. Among non-smokers, recurrence was observed in 48 (25.4%), while 141 (74.6%) had no recurrence (p = 0.052).

Tumor-related variables highlighted critical findings. Recurrence was higher in patients with ER/PR-negative hormone receptor status, with 36 (39.1%) experiencing recurrence and 56 (60.9%) with no recurrence. Conversely, ER/PR-positive patients had a significantly lower recurrence rate, with 46 (24.2%) experiencing recurrence and 144 (75.8%) showing no recurrence (p = 0.010). HER2 status, lymph node involvement, and tumor stage did not show significant associations with recurrence, as their p-values were above the threshold of 0.05. Lastly, recurrence type was significantly associated with recurrence status (p =0.000), as 38 (100%) local recurrences, 31 (100%) regional recurrences, and 13 (100%) distant recurrences occurred exclusively among the recurrence group. (Table 2)

Table 1: Recurrence status and survival status

Variable	Category	Frequency (n)	Percent (%)
	No recurrence	200	70.9
Recurrence Status	Recurrence	82	29.1
	Total	282	100.0
Overall Survival Status	Alive	223	79.1
	Death	59	20.9
	Total	282	100.0

Variable	Category	No Occurrence n (%)	Occurrence n (%)	Total (n)	p-value
Age	Less than 50 years	99 (70.21%)	42 (29.79%)	141	
	50 years or above	101 (71.63%)	40 (28.37%)	141	
Menopausal Status	Pre-menopausal	75 (65.22%)	40 (34.78%)	115	0.080
	Post-menopausal	125 (74.85%)	42 (25.15%)	167	
Obesity	Non-obese	132 (69.84%)	57 (30.16%)	189	0.569
	Obese	68 (73.12%)	25 (26.88%)	93	
Smoking Status	Non-smoker	141 (74.60%)	48 (25.40%)	189	
	Smoker	59 (63.44%)	34 (36.56%)	93	
Histological Grade	Grade I	61 (70.11%)	26 (29.89%)	87	0.707
	Grade II	100 (72.99%)	37 (27.01%)	137	
	Grade III	39 (67.24%)	19 (32.76%)	58	
Hormone Receptor Status	ER/PR-Negative	56 (60.87%)	36 (39.13%)	92	0.010
	ER/PR-Positive	144 (75.79%)	46 (24.21%)	190	
HER2 Status	Positive	41 (69.49%)	18 (30.51%)	59	0.786
	Negative	159 (71.30%)	64 (28.70%)	223	
Lymph Node Involvement	Yes	74 (69.16%)	33 (30.84%)	107	0.610
	No	126 (72.00%)	49 (28.00%)	175	
Tumor Stage	Stage I	67 (69.79%)	29 (30.21%)	96	0.950
	Stage II	89 (71.77%)	35 (28.23%)	124	
	Stage III	44 (70.97%)	18 (29.03%)	62	
Recurrence Type	No recurrence	200 (100%)	0 (0%)	200	0.000
	Local recurrence	0 (0%)	38 (100%)	38	
	Regional recurrence	0 (0%)	31 (100%)	31	
	Distant recurrence	0 (0%)	13 (100%)	13	

#### DISCUSSION

This study investigated the frequency of breast cancer recurrence and its influencing factors, reporting a recurrence rate of 29.1% and a survival rate of 79.1%. These findings contribute to the growing evidence on breast cancer outcomes and align with prior studies on recurrence patterns and prognostic factors.

The recurrence rate of 29.1% observed in this study is consistent with the findings of Courtney et al., who reported

recurrence rates of 25–30%, reflecting the persistent challenges in managing breast cancer recurrence despite advancements in treatment<sup>11</sup>. Abdulwassi et al. similarly noted high recurrence rates, particularly in younger patients, and emphasized the association between higher TNM stages and worse disease-free survival<sup>12</sup>. The overall survival rate of 79.1% in this study aligns with prior research, such as Sopik et al., who reported a 10-year survival rate of 71% post-local recurrence, highlighting the importance of long-term follow-up<sup>13</sup>.

Younger age (<50 years) was associated with a slightly higher recurrence rate in this study, though the difference was not statistically significant (p = 0.793). Similar findings were reported by Abdulwassi et al., where younger women demonstrated worse outcomes due to more aggressive tumor subtypes<sup>12</sup>. Premenopausal women also showed a higher recurrence rate (34.8%) compared to postmenopausal women (25.1%), consistent with findings by Lafourcade et al., who highlighted the role of hormonal changes and receptor status in recurrence risk<sup>14</sup>.

Smoking status was found to have a borderline significant association with recurrence (p = 0.052), with smokers experiencing a higher recurrence rate (36.6%) compared to non-smokers (25.4%). Lafourcade et al. also identified smoking as a key factor in increasing relapse risk, supporting the need for lifestyle interventions to improve outcomes<sup>14</sup>.

Tumor-related factors had significant implications for recurrence in this study. Hormone receptor-negative tumors were associated with a significantly higher recurrence rate (39.1%) compared to hormone receptor-positive tumors (24.2%) (p = 0.010). This finding aligns with Shahriari-Ahmadi et al., who reported that ER/PR-negative status is a strong predictor of early recurrence due to the aggressive nature of these tumors<sup>15</sup>.

HER2 status, although not statistically significant in this study, has been previously shown to influence recurrence rates. O'Shaughnessy et al. emphasized that HER2-positive breast cancer is associated with higher recurrence rates in the absence of targeted therapies, although the introduction of trastuzumab has significantly improved outcomes<sup>16</sup>.

The significant association between recurrence type (local, regional, distant) and recurrence status (p = 0.000) in this study underscores the importance of understanding recurrence patterns. Pogoda et al. highlighted that TNBC patients often experience distinct patterns of early recurrence, with metastases frequently occurring in the brain and lungs<sup>17</sup>. Recognizing such patterns enables more personalized follow-up strategies and treatment protocols.

Although imaging parameters were not assessed in this study, Lee et al. demonstrated the value of advanced imaging techniques, such as MRI, in predicting recurrence risk. Features like increased ipsilateral vascularity and skewness in texture analysis were significantly associated with recurrence, suggesting the potential for integrating imaging biomarkers into routine follow-up<sup>18</sup>.

The psychological impact of breast cancer recurrence is significant, as highlighted by Kussainova et al., who identified fear of recurrence as a major concern affecting patient quality of life. Addressing this through interventions like mindfulness and cognitive-behavioral therapy can improve psychological outcomes and potentially influence compliance with follow-up care<sup>19</sup>.

The findings of this study highlight the need for stratified management based on recurrence risk factors, such as hormone receptor status, menopausal status, and lifestyle factors like smoking. Personalized treatment plans, incorporating advancements in targeted therapies and imaging techniques, are essential to improving outcomes. Additionally, addressing psychosocial factors and promoting lifestyle modifications should be integral to survivorship care.

#### CONCLUSION

This study highlights the significant burden of breast cancer recurrence, with a recurrence rate of 29.1% and a survival rate of

79.1%. Factors such as hormone receptor-negative status, premenopausal state, and smoking were associated with higher recurrence risk, emphasizing the need for tailored follow-up and management strategies. While advancements in treatment, particularly for HER2-positive and hormone receptor-positive tumors, have improved outcomes, the persistent risk of recurrence and its impact on survival underscore the importance of stratified care. Addressing modifiable risk factors and implementing personalized surveillance protocols could further enhance long-term outcomes for breast cancer patients.

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