



## Disease Failure Patterns and Survival Outcomes in Treated Breast Cancer Patients from a Rural Cancer Centre in Maharashtra, India

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### ABSTRACT

#### Background :

Breast cancer is a biologically heterogeneous malignancy and a major cause of morbidity and mortality among women. Disease failure in the form of locoregional recurrence and distant metastasis continues to adversely affect survival outcomes despite advances in multimodality treatment. Evaluation of patterns of disease failure and survival following recurrence is essential for understanding disease outcomes.

#### Methods:

This longitudinal observational study was conducted at a tertiary care rural centre and included previously treated patients with carcinoma breast who were followed up over time. Patients who developed disease failure during follow-up were analysed. Demographic, clinicopathological, molecular, and treatment-related variables were recorded. Disease failure was classified as locoregional, distant, or combined. Survival outcomes were assessed descriptively using Kaplan–Meier analysis.

#### Results :

A total of 21 cases were evaluated for disease failure during the study period. Most patients presented with advanced-stage disease, with 14 patients (66.7%) having Stage III disease, and aggressive molecular subtypes were common, including 8 patients (38.1%) with triple-negative disease and 4 patients (19.0%) with HER2-enriched tumours. Early disease failure occurred in 11 patients (52.4%) within one year. Distant metastasis was the predominant pattern of failure in 14 patients (66.7%), followed by combined locoregional and distant failure in 5 patients (23.8%), while isolated locoregional recurrence was infrequent in 2 patients (9.5%) and showed better survival outcomes. Post-recurrence treatment was predominantly palliative, with systemic therapy administered in 15 patients (71.4%) and radiotherapy in 13 patients (61.9%). Survival after recurrence was poor, with mortality

observed in 9 patients (42.9%) at last follow-up, particularly among those with early relapse and aggressive tumour biology. The median disease-free survival was 20 months, with a median post-recurrence survival of 8 months and a median overall survival of 2 years 9 months.

#### Conclusion :

Disease failure following treatment of carcinoma breast was commonly observed in patients with advanced-stage disease and aggressive molecular subtypes. Early recurrence and distant metastasis were associated with poorer survival outcomes. Optimizing primary treatment, close follow-up, and appropriate salvage approaches remain important in patients with recurrent breast cancer, especially in resource-limited settings.

**Keywords:** Breast cancer, disease failure, recurrence, survival outcomes, salvage treatment

### I. INTRODUCTION

Breast cancer is the most commonly diagnosed malignancy among women worldwide and remains a leading cause of cancer-related morbidity and mortality [1]. According to global cancer statistics, breast cancer accounts for a substantial proportion of newly diagnosed cancers, with an increasing burden in low- and middle-income countries [1,2]. In India, the incidence of breast cancer has been rising steadily, with a significant number of patients presenting at a younger age and with advanced-stage disease [2]. Despite advances in early detection and multimodality treatment, disease failure following definitive therapy continues to pose a major clinical challenge [14].

Disease failure in carcinoma breast may manifest as locoregional recurrence, distant metastasis, or a combination of both and is a critical determinant of long-term survival [12]. Recurrence risk is influenced by stage at diagnosis, tumor biology and molecular subtype, adequacy of surgery, and compliance with adjuvant systemic



therapy and radiotherapy[3,6]. Aggressive molecular subtypes such as triple-negative and HER2-enriched breast cancers are associated with higher recurrence rates, earlier disease failure, and poorer survival outcomes compared to hormone receptor-positive disease [4,13].

In rural and resource-limited settings, additional challenges such as delayed diagnosis, restricted access to advanced diagnostic facilities, financial limitations, and treatment non-compliance further contribute to adverse outcomes. Data describing patterns of disease failure and survival outcomes in previously treated carcinoma breast patients from rural cancer centres in India remain limited. The present longitudinal observational study was undertaken to evaluate patterns of disease failure, clinicopathological characteristics, treatment compliance, and survival outcomes in previously treated carcinoma breast patients at a rural cancer centre in Maharashtra, India.

## II. MATERIALS AND METHODS

This descriptive longitudinal observational study was conducted in the Department of Radiation Oncology at DBVVP Pravara Rural Hospital, a tertiary care rural cancer centre in Maharashtra, India, between January 2024 and December 2025. The study included histopathologically confirmed female patients with carcinoma breast who were non-metastatic at initial diagnosis and subsequently developed disease failure during follow-up after definitive treatment. Approval was obtained from the Institutional Ethics Committee, and written informed consent was taken from all participants in the local language.

All eligible patients presenting to the Oncology department during the first 18 months of the study period were included using a universal sampling method. Patients had previously undergone surgery for the primary disease, either breast-conserving surgery or modified radical mastectomy with axillary lymph node dissection, followed by neoadjuvant and/or adjuvant chemotherapy, radiotherapy, targeted therapy, and/or hormonal therapy as indicated.

Demographic, clinical, and histopathological variables including age, tumor characteristics, stage, treatment details, margin status, nodal involvement, lymphovascular and perineural invasion, and extracapsular extension were recorded. Molecular subtyping was based on immunohistochemical evaluation of estrogen receptor, progesterone receptor, and HER2/neu status, classifying tumours as luminal A, luminal B, HER2-enriched, or triple-negative.

Disease-free survival was defined as the interval between completion of primary treatment and detection of disease failure. Patients presenting with recurrence underwent thorough clinical evaluation, imaging, and biopsy where feasible. Recurrence was classified as locoregional, distant, or combined, and restaging was performed according to the AJCC 8th edition TNM staging system.

Post-recurrence management intent was categorized as curative or palliative. Treatment decisions were individualized based on patient performance status, disease extent, prior therapies, and available treatment options, including surgery, radiotherapy, systemic therapy, hormonal therapy, and HER2-targeted therapy. Patients were followed up clinically and radiologically, and treatment response was assessed using RECIST version 1.1. Post-recurrence survival and overall survival were recorded until death or last follow-up. Statistical analysis was descriptive, and survival outcomes were estimated using the Kaplan–Meier method.

## III. OBSERVATIONS AND RESULTS

### Patient Characteristics

The study included 21 histopathologically confirmed female patients with carcinoma breast who were non-metastatic at initial diagnosis and subsequently developed disease failure during follow-up. Patient age ranged from 32 to 71 years, with the most common age group being 41–50 years (42.9%). Patients aged  $\leq 40$  years and  $>60$  years each constituted 23.8% of the cohort. Comorbidities were present in 9.5% of patients, while 90.5% had no associated medical illness. Mishri use was reported in 23.8% of patients, and a positive family history of malignancy was noted in 14.3%. Postmenopausal women comprised 52.4% of the study population (Table 1).

### Clinicopathological Characteristics

Invasive ductal carcinoma was the predominant histological subtype, seen in 20 patients (95.2%). High-grade tumours were common, with Grade III disease observed in 19 patients (90.5%). At presentation, all patients had non-metastatic disease. T2 tumours were most frequent, seen in 14 patients (66.7%), and nodal involvement was present in 18 patients (85.7%). Stage III disease predominated in 14 patients (66.7%), with Stage IIIC being the most common subgroup, observed in 8 patients (38.1%) (Table 1).



### Molecular Subtypes

Triple-negative breast cancer was the most common molecular subtype, observed in 8 patients (38.1%) (ER-, PR-, HER2-). Luminal B tumours accounted for 5 patients (23.8%) (ER+, PR+, HER2+ or ER+, PR-, HER2±), followed by luminal A subtype in 4 patients (19.0%) (ER+, PR+, HER2-). HER2-enriched tumours were also seen in 4 patients (19.0%) (HER2+, ER-, PR-), as shown in Table 1. Overall, hormone receptor positivity was observed in 9 patients (42.9%). BRCA mutation testing was performed in 5 patients (23.8%), and all tested individuals were found to be BRCA-negative.

Adjuvant radiotherapy was completed in 17 patients (81.0%), while 4 patients (19.0%) defaulted. Chemotherapy was administered in 15 patients (71.4%), with adjuvant chemotherapy alone being the most frequent approach. Chemotherapy compliance was satisfactory in 15 patients (71.4%), while 2 patients (9.5%) received incomplete treatment. Targeted therapy with trastuzumab was indicated in 8 HER2-positive patients, but regular completion was achieved in only 1 patient. Hormonal therapy was administered in 7 patients (33.3%), with poor compliance noted in the majority (Table 2).

Characteristic	Category	n [%]
Age group [years]	≤40	5 [23.8]
	41–50	9 [42.9]
	51–60	2 [9.5]
	>60	5 [23.8]
Menopausal status	Premenopausal	10 [47.6]
	Postmenopausal	11 [52.4]
Histological grade	Grade II	2 [9.5]
	Grade III	19 [90.5]
Overall stage	Stage II	7 [33.3]
	Stage III	14 [66.7]
Molecular subtype	Luminal A	4 [19.0]
	Luminal B	5 [23.8]
	HER2-enriched	4 [19.0]
	Triple-negative	8 [38.1]
Surgical margins	Negative	18 [85.7]
	Positive	3 [14.3]
Lymphovascular invasion	Present	9 [42.9]
	Absent	12 [57.1]
Perineural invasion	Present	5 [23.8]
	Absent	16 [76.2]
Extranodal extension	Present	9 [42.9]
	Absent	12 [57.1]

Table 1. Baseline Demographic and Clinicopathological Characteristics of the Study Population

### Primary Treatment and Compliance

Modified radical mastectomy with axillary lymph node dissection was performed in 19 patients (90.5%). Surgical margins were negative in 18 patients (85.7%). Lymphovascular invasion and perineural invasion were present in 9 patients (42.9%) and 5 patients (23.8%), respectively.



Treatment modality	Status	n [%]
Type of surgery	Modified radical mastectomy	19 [90.5]
	Breast-conserving surgery	2 [9.5]
Chemotherapy	Received regularly	15 [71.5]
	Irregular / incomplete	2 [9.5]
	Not received	4 [19.0]
Hormonal therapy (n = 8)	Received regularly	2 [25.0]
	Irregular / incomplete	5 [62.5]
	Defaulted	1 [12.5]
Targeted therapy – trastuzumab (n = 8)	Completed	1 [12.5]
	Incomplete	2 [25.0]
	Defaulted	5 [62.5]

Table 2: Primary Treatment Modalities and Compliance Status

### Disease-Free Survival

Disease-free survival ranged from 1 month to 9 years, with a median of 20 months. Early disease failure within one year was observed in 11 patients (52.4%). Median disease-free survival was longer in Stage II disease compared to Stage III and was highest in luminal A tumours, seen in 4 patients, with a median of 4 years (3 years 6 months to 9 years). Luminal B tumours, seen in 5 patients, showed a median disease-free survival of 1 year 6 months (6 months to 5 years). HER2-enriched tumours, seen in 4 patients, had a median disease-free survival of 9 months (1 month to 1 year 8 months), while triple-negative breast cancer, seen in 8 patients, demonstrated the shortest disease-free survival, with a median of 6 months (1 month to 12 months). The distribution of disease-free survival according to stage at diagnosis and molecular subtype is depicted in Figure 1.

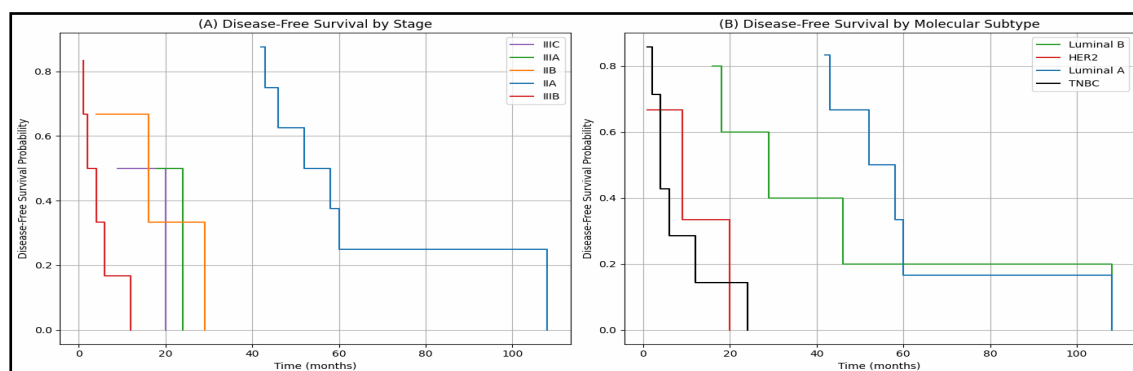


Figure 1: Kaplan–Meier curves depicting disease-free survival (DFS) according to (A) stage at diagnosis and (B) molecular subtype among treated carcinoma breast patients.

Median disease-free survival was 1 year 8 months in 15 patients receiving regular chemotherapy, 6 months in 2 patients receiving irregular chemotherapy, and 1 year in 4 patients defaulting chemotherapy. The patient completing targeted

therapy (1 patient) demonstrated a disease-free survival of 9 years, while disease-free survival ranged from 1 month to 3 years 10 months in patients receiving irregular targeted therapy and from 2 months to 5 years in patients defaulting targeted therapy. Regular hormonal therapy showed



disease-free survival up to 4 years in patients receiving regular therapy, compared with 1 year in patients receiving irregular therapy and 2 months in patients defaulting therapy. The calculated disease-free survival across clinicopathological subgroups is shown in Figure 2.

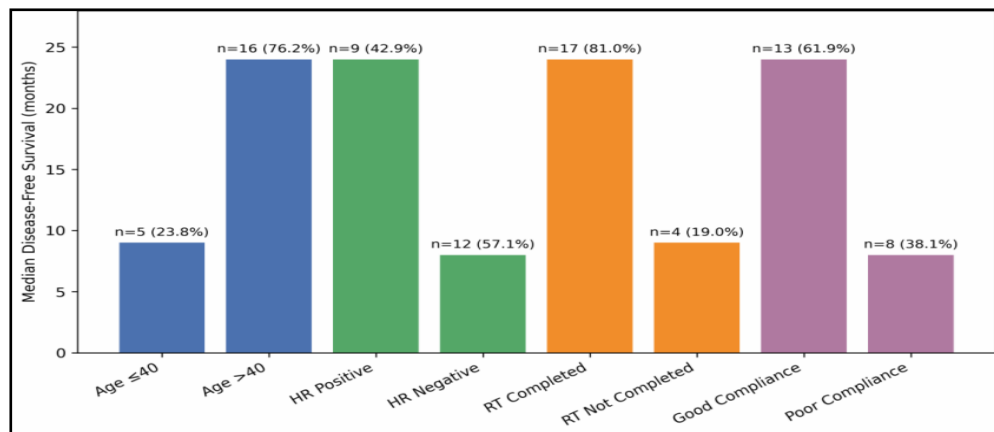


Figure 2: Distribution of Median Disease-Free Survival Across Clinicopathological Subgroups

### Patterns of Disease Failure

Distant metastasis was the predominant pattern of disease failure, observed in 14 patients (66.7%). Combined locoregional and distant failure occurred in 5 patients (23.8%), while isolated locoregional recurrence was noted in 2 patients (9.5%). The distribution of disease failure patterns is illustrated in Figure 3. Among locoregional recurrences, regional nodal involvement was most common. Sites of distant metastasis included liver, bone, and nodal involvement in 9 patients each (47.4%), followed by lung metastasis in 7 patients (36.8%) and brain metastasis in 5 patients (26.3%). Contralateral breast involvement was observed in 3 patients (15.8%). Stage IV disease was present in 19 patients (90.5%), whereas Stage IIIC and Stage IIIB disease were each noted in 1 patient (4.8%). Among patients completing radiotherapy (17 patients), locoregional failure occurred in 5 patients (29.4%) and distant failure in 16 patients (94.1%), with a median disease-free survival of 2 years, compared with 2 patients (50.0%) and 3 patients (75.0%), respectively, among those defaulting radiotherapy (4 patients), who had a median disease-free survival of 9 months.

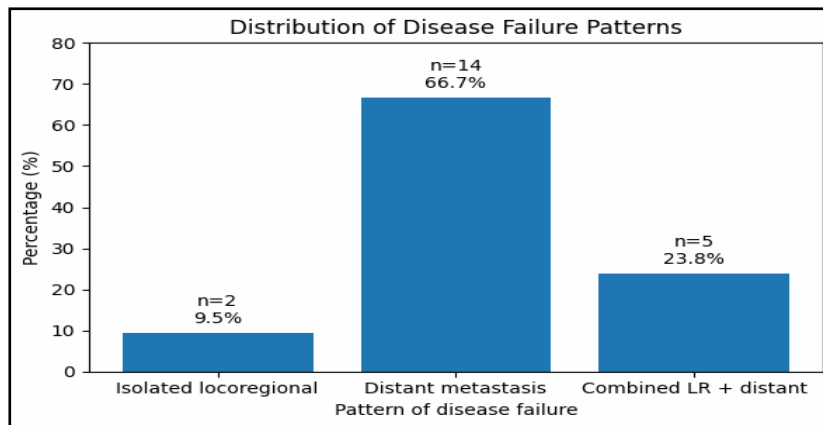


Figure 3: Distribution of Disease Failure Patterns

### Management of disease failure

Surgical salvage was feasible in only 2 patients (9.5%), both with isolated locoregional recurrence. Radiotherapy for recurrence was administered in 13 patients (61.9%), predominantly for palliation, most commonly for brain metastases and skeletal lesions. Chemotherapy for recurrent disease was given in 15 patients (71.4%). Targeted therapy and hormonal therapy were administered selectively based on receptor status, prior treatment exposure, and patient fitness, with targeted therapy used in 4 patients (19.0%) and hormonal therapy in 8 patients (38.1%).

### Survival Outcomes

Response evaluation using RECIST 1.1 criteria showed partial response in 13 patients (61.9%) at 1.5 months, while complete response was uncommon. At last follow-up, 12 patients (57.1%) were alive, while 9 patients (42.9%) had expired. Post-recurrence survival ranged from 1 month to 1 year 8 months, with a median of 8 months. Overall survival ranged from 1 year to 9 years 7 months, with a median overall survival of 2 years 9 months. Patients with isolated locoregional recurrence demonstrated better post-recurrence and overall survival compared to those with distant or combined patterns of failure, as illustrated in the Kaplan–Meier survival curves (Figure 4).

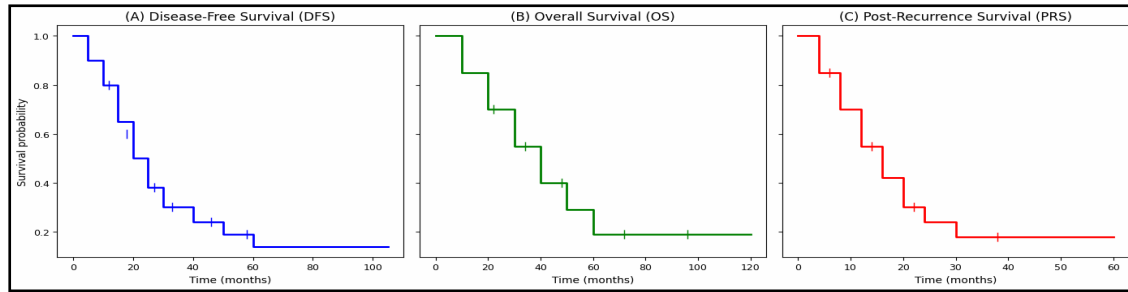


Figure 4: Kaplan–Meier survival curves depicting [A] disease-free survival [DFS], [B] overall survival [OS], and [C] post-recurrence survival [PRS] among treated carcinoma breast patients.

Among 21 patients with recurrence, DFI  $\leq 12$  months was seen in 11 (52.4%) with median PRS/OS of 6 months/2 years and DFI  $> 12$  months in 10 (47.6%) with 3 years 6 months/4 years 9 months; locoregional-only recurrence occurred in 2 (9.5%) with 3 years 6 months/6 years and distant  $\pm$  locoregional recurrence in 19 (90.5%) with 8 months/2 years 7 months, including bone-only metastasis in 4 (28.6%) with 1 year 2 months/4 years 9 months and visceral/brain metastasis in 10 (71.4%) with 6 months/2 years 2 months; molecular subtypes were Luminal A 4 (19.0%) with 4 years/6 years 6 months, Luminal B 5 (23.8%) with 1 year 6 months/3 years 10 months, HER2-enriched 4 (19.0%) with 9 months/3 years 3 months, and triple-negative 8 (38.1%) with 6 months/1 year 8 months, and hormone receptor positivity in 9 (42.9%) with 2 years/4 years 9 months versus negativity in 12 (57.1%) with 8 months/2 years. Post-recurrence and overall survival according to clinicopathological and treatment-related factors are illustrated in Figure 5.

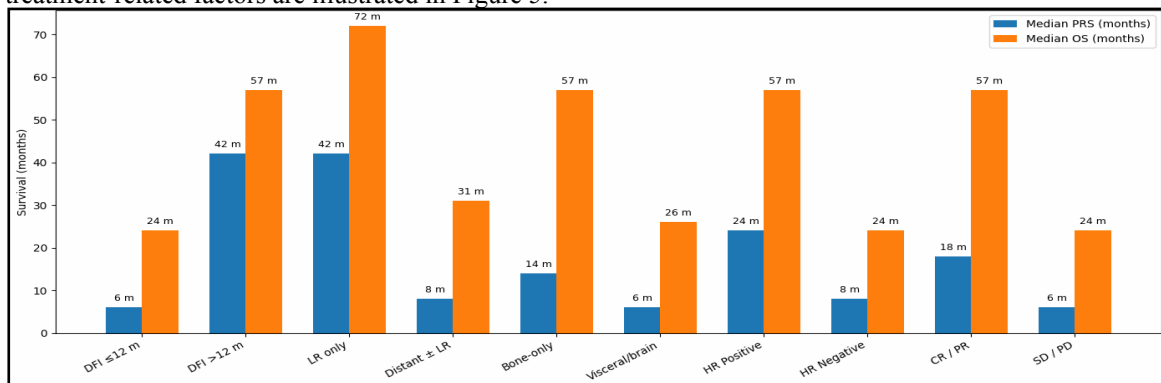


Figure 5: Post-Recurrence and Overall Survival According to Clinicopathological and Treatment-Related Factors

## V. DISCUSSION

Breast cancer continues to represent a major global health burden, with disease recurrence remaining a key contributor to cancer-related morbidity and mortality despite advances in

## IV.

multimodality treatment [1,14]. The present observational study from a rural cancer centre in Maharashtra provides real-world insight into disease failure patterns, clinicopathological characteristics, treatment compliance, and survival outcomes in



previously treated carcinoma breast patients who developed recurrence after definitive therapy. The findings highlight the combined influence of aggressive tumour biology and suboptimal treatment compliance on recurrence and survival outcomes in a resource-limited rural setting.

In the present cohort, a high proportion of patients presented with advanced disease, with Stage III disease observed in 66.7% of cases. This pattern is consistent with reports from the National Cancer Registry Programme of India, which document delayed presentation and a predominance of advanced-stage breast cancer in rural populations [2]. Factors such as limited awareness, socioeconomic constraints, lack of organized screening, and delays in referral to specialized oncology centres contribute to this trend. Advanced stage at diagnosis has been consistently associated with higher recurrence rates and inferior survival, as demonstrated in large meta-analyses by the Early Breast Cancer Trialists' Collaborative Group (EBCTCG) [12].

The molecular classification of breast cancer described by Perou et al. established the prognostic and therapeutic relevance of intrinsic subtypes [3,13]. In the present study, triple-negative breast cancer demonstrated the shortest disease-free survival, reflecting its aggressive clinical course, early relapse, and limited therapeutic options, as also reported by Foulkes et al. [4]. HER2-enriched tumours showed inferior outcomes in patients who did not receive or complete targeted therapy, emphasizing the established survival benefit of trastuzumab in HER2-positive disease [5,16]. In contrast, luminal A tumours demonstrated more favourable disease-free and post-recurrence survival, underscoring the prognostic importance of hormone receptor positivity [13,14].

Histopathological factors further contributed to adverse outcomes in this cohort. A predominance of high-grade tumours was observed, with Grade III disease present in more than 90% of patients. High histological grade has been consistently associated with aggressive tumour behaviour and increased risk of recurrence [3,14]. Adverse pathological features such as lymphovascular invasion, nodal positivity, and extranodal extension were also common and have been recognized as predictors of both locoregional and distant failure in large pooled analyses [12]. The high prevalence of extranodal extension in this study further reflects the biologically aggressive nature of the disease in this population.

Treatment compliance played a critical role in determining outcomes. Although most patients underwent appropriate surgical management,

adherence to adjuvant radiotherapy, chemotherapy, targeted therapy, and hormonal therapy was suboptimal. Nearly one-fifth of patients defaulted radiotherapy, and completion of systemic therapy was inconsistent, particularly for trastuzumab and hormonal therapy. Inadequate delivery of systemic therapy has been associated with early recurrence and reduced survival, as demonstrated in landmark trials and guideline-based analyses [5,12,18]. Financial constraints and limited access to targeted agents were major contributors to treatment default in this rural cohort.

Early recurrence is a recognized marker of aggressive tumour biology and poor prognosis [17]. The relatively short median disease-free survival observed in this study further reflects the impact of aggressive tumor biology and incomplete adjuvant therapy. Patients with a shorter disease-free interval demonstrated poorer post-recurrence and overall survival, consistent with population-based analyses [17].

Distant metastasis was the predominant pattern of disease failure, while isolated locoregional recurrence was uncommon. Similar patterns have been reported in large meta-analyses and population-based studies, which emphasize distant metastasis as the most common mode of failure in high-risk breast cancer patients [12,17]. Visceral and brain metastases were particularly frequent in HER2-enriched and triple-negative subtypes, a distribution that has been associated with inferior survival outcomes [15,17].

Salvage treatment options were limited, largely due to advanced disease at recurrence and compromised performance status. Surgical salvage was feasible only in patients with isolated locoregional recurrence and was associated with more favourable outcomes, consistent with reports supporting aggressive local therapy in carefully selected patients [12]. Most patients required palliative treatment, with radiotherapy and chemotherapy providing symptom control but limited impact on long-term survival, as reported in prior studies [10,17].

Post-recurrence survival in this cohort was poor, reflecting the advanced nature of disease at recurrence. Better outcomes were observed in patients with isolated locoregional recurrence, hormone receptor-positive disease, longer disease-free intervals, and good treatment compliance, findings consistent with established prognostic models [12,14]. Conversely, triple-negative disease, early recurrence, visceral or brain metastases, and poor compliance were associated with inferior survival [4,15,17].



The rural setting adds important context to these findings. Limited access to advanced diagnostics, financial toxicity, irregular follow-up, and treatment default were common challenges, as also highlighted in Indian cancer registry data and clinical guidelines [2,18]. These factors underscore the need for improved patient education, strengthened follow-up systems, and better access to guideline-recommended therapies in rural cancer care.

Despite limitations such as small sample size and single-centre design, this study provides meaningful real-world insight into disease failure patterns and survival outcomes among treated carcinoma breast patients from a rural Indian cancer centre.

The findings underscore the combined impact of aggressive tumour biology and suboptimal treatment compliance on recurrence patterns and survival outcomes in a resource-limited rural setting. Early recurrence and distant metastasis emerged as the predominant patterns of failure and were associated with poor survival [12,17]. These observations highlight the need to improve treatment compliance and access to effective systemic therapies in such settings [18].

## VI. CONCLUSION

This descriptive longitudinal study provides important insights into disease failure patterns, treatment approaches, and survival outcomes in previously treated breast carcinoma patients from a rural tertiary care centre. Most patients presented with advanced-stage, high-grade disease and aggressive molecular subtypes, resulting in a high rate of early recurrence. Distant metastasis was the most common pattern of failure, while isolated locoregional recurrence was uncommon but associated with better survival, suggesting a potential role for salvage local therapy in selected patients.

Treatment compliance emerged as a major determinant of outcomes. Completion of adjuvant radiotherapy, chemotherapy, targeted therapy, and hormonal therapy was associated with improved survival, whereas treatment default and irregular follow-up—often related to socioeconomic and access barriers—contributed to poor disease control. Management of recurrent disease was largely palliative, with limited durable responses. Overall, these findings highlight the interplay between tumor biology, stage at diagnosis, treatment adherence, and healthcare accessibility. Strengthening early detection, ensuring completion of guideline-based multimodality treatment, improving follow-up

adherence, and expanding access to systemic therapies are essential to improve outcomes in breast cancer patients, particularly in resource-limited rural settings.

## VII. LIMITATIONS

The longitudinal observational design, small sample size, and single-center nature of this study may limit the generalizability of the findings. The absence of multivariate analysis and limited access to advanced molecular profiling further restrict detailed prognostic evaluation. Nevertheless, the study provides meaningful real-world insights into disease failure patterns and survival outcomes in treated carcinoma breast patients from a rural, resource-constrained setting.

### Declaration of Patient Consent

The authors certify that appropriate patient consent was obtained for publication of clinical information and images. Patient identities will not be disclosed, and all reasonable efforts will be made to maintain anonymity, although complete anonymity cannot be guaranteed.

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Nil.

### Conflicts of interest

There are no conflicts of interest.

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