



## A TEN YEARS RETROSPECTIVE EVALUATION OF CLINICAL AND TREATMENT OUTCOME OF CARCINOMA BREAST

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### ABSTRACT

**Background:** Breast cancer most often begins with cells in the milk-producing ducts (invasive ductal carcinoma). Breast cancer may also begin in the glandular tissue called lobules (invasive lobular carcinoma) or in other cells or tissue within the breast.

Breast cancer is the most common cancer in women overall. Globally, breast cancer now represents one in four of all cancers in women.

This study is the evaluation OF CLINICAL AND TREATMENT OUTCOME OF CARCINOMA BREAST<sup>®</sup> on the basis of patient's characteristic distribution, disease characteristics, management and follow up.

**Aims And Objective-** The aim of this study is to evaluate patient's characteristic distribution, disease characteristics, management and follow up. The objective of this study is retrospective evaluation of all patients with carcinoma breast registered in Radiation Oncology Department at GMC, Bhopal in last ten years. **Material And Method-** This retrospective analytical study was included 1061 patients of breast cancer registered at Department of Radiation Oncology, Gandhi Medical College and Hamidia Hospital Bhopal in last ten years from 2010 to 2019. Data would include total number of patients of carcinoma breast registered; proportion of breast cancer cases treated by chemotherapy and radiotherapy. Patient details: Name, age, sex, Hormonal receptor status, Histopathology details and TNM stage with stage group, Menstrual status 5) Family history, Treatment strategy, details of treatment and compliance to treatment, Response to treatment using RECIST criteria, Details of follow up at 3 month, 6 months, 1 year. Treatment outcome in terms of no abnormality detected, relapse, recurrence or residual disease. **Result** – Average age was observed to be 47.36 years with SD of 11.66. Maximum number of the patients presented with IIIA stage (44.2%), maximum number of patients were having IDC (infiltrating ductal carcinoma) or IVC (invasive ductal carcinoma) (84.07%). The hormonal receptors ER receptors were observed in majority of the patients with 38.54%, Only 3.01% patients having significant family history, majority of patients 56.83% were belonging to premenopausal group. Nearly 154 patients were having metastasis at various sites out of which 62.9% Bone metastasis followed by 24.6% lung metastasis. Maximum number of patients were treated with Chemotherapy (84.8%) followed by surgery with nearly (76.3%) of the patients. Patients were treated as hormonal therapy with majority of Letrozole 27.5%, followed by Anastrozole 7.06%. Average of 699.3 with SD of 169.99 patients have been followed up for the mean time period of 6 months, and nearly 18.57% patients showed the negative response in follow up. Majority of the patients were observed in PR with 46.5% volume. **Conclusion-** Breast cancer is the most common malignancies prevalent in India in female and are major public health burden. Incidence of breast cancer are increasing because of lack of awareness, increasing with age. Majority of the patients present at locally advanced stage hence neoadjuvant chemotherapy plays an important role in downstaging the tumour. Standard follow-up of patients treated for breast cancer is based on regular follow-up visits, with frequency decreasing in consecutive years.

### KEYWORDS :

#### INTRODUCTION

Breast cancer is the most frequently diagnosed public health trouble and accounts for one-third of cancer cases in female throughout the world. Breast cancer in female is the highest burden estimated to make a contribution 2,00,000 (14.8%) of the total cancer cases.[1,2]. In INDIA irrespective of the gender, breast cancer is the most commonly diagnosed malignancy, with incidence of 13.5% (178361 cases) and death rate of 10.6% (90,408 deaths) being highest among all cancers. However in females the incidence is (26.3%) (3)

Metastasis ailment remains the underlying cause of loss of life in the majority of breast cancer patients who succumb to their sickness.[4]

The distant organs to which breast cancers most commonly metastasized are bone, liver, lung and brain. These sites are of scientific and organic importance and closely related to the patient's survival consequences.[2,5]

Risk factors associated with breast cancer are increasing age, low parity, obesity, age at marriage, age at first childbirth and age at menarche. (6-11). In 5% of carcinoma cases, there is a robust inherited familial risk. It includes mutations in BRCA1, BRCA2, P53, PTEN and ATM genes. (12).

The prognostic factors associated with breast cancer include tumor size, lymph node involvement, lympho-vascular invasion, proliferative rate (ki 67 index), histologic type, grade, stage at presentation, expression of ER, PR, & HER2 neu status.(13).

Breast cancer patients require multimodality treatment including surgery, radiotherapy, chemo therapy along with hormonal and targeted therapy. For localised breast cancers, breast conservation surgery followed by radiation to whole breast or mastectomy followed by chest wall irradiation may be considered, depending on tumor size, margin and lymph node status.. Hormonal therapy based on receptor status is also an essential component of breast cancer treatment.(14) In recent years, the molecular mechanisms driving the heterogeneous treatment response in breast cancer have been better elucidated.. The aim of developing these agents is treatment of specific molecular subtype of breast cancer. Treatment options should be tailored to individual patient accordingly.(15-16)

Radiotherapy (RT) is a crucial component of breast cancer treatment. Whole breast RT after lumpectomy and chest wall RT after mastectomy both have shown improved loco-regional control and definitive survival benefit. Tangential opposed beam to chest wall or whole breast is standard field for conventional planning. With the advancements of technology, there is a gradual shift from 2D to 3D and recently 4D techniques. The aim of all the newer techniques being improved tumor control and decreased side effects..(17-18).

#### MATERIAL AND METHOD -

This retrospective analytical study was included 1061 patients of breast cancer registered at Department of Radiation Oncology, Gandhi Medical College and Hamidia Hospital Bhopal in last ten years from 2010 to 2019.

**Study Design-**

Retrospective analytical study Study Area- Department of Radiation oncology, Gandhi Medical College and associated Hamidia Hospital, Bhopal Study duration- July 2019 to July 2021.

**Inclusion Criteria-**

For inclusion in the study patient must fulfill all of the following criteria – Histopathologically confirmed cases of carcinoma breast. Patients document and case history present in Department . Age group between 15 to 80 years.

**Exclusion Criteria -**

Age below 15 years . No histopathology report . Age above 80 years .

**METHODOLOGY -**

Data retrieval- by browsing case files made in opd after registration. Data would include total number of patients of carcinoma breast registered; proportion of breast cancer cases treated by chemotherapy and radiotherapy.

- 1.) Patient details: Name, age, sex, residence(rural/urban)
- 2) Hormonal receptor status
- 3.) Histopathology details and TNM stage with stage group.
- 4) Menstrual status
- 5) Family history
- 6.) Treatment strategy, details of treatment and compliance to treatment.
- 7.) Response to treatment using RECIST criteria.
- 8.) Details of follow up at 3 month, 6 months, 1 year .
- 9) Treatment outcome in terms of no abnormality detected, relapse, recurrence or residual disease.

**Work-up Protocol –**

CBC, Platelet, LFT, RFT, Serum Protein, Serum Electrolytes, Chest X-Ray, CECT Scan Breast (Chest), MRI (If available) ER/PR/Her2 Status, Bone scan (if available), ECG, 2D Echo, PET CT Scan (if available)

**Staging Protocol –**

TNM staging was done as per American joint committee on cancer (AJCC) 8th edition (2018).

**Treatment Protocol –**

1.) The protocol followed in Department was neoadjuvant chemotherapy followed by surgery followed by radiotherapy followed by adjuvant chemotherapy followed by hormonal or targeted therapy

2.) Metastatic cases were treated symptomatically or with palliative chemotherapy and/or radiotherapy.

**Response Assessment Protocol-**

Patients were evaluated at three weekly intervals during chemotherapy and weekly during radiotherapy. Complete blood count along with clinical examination was performed. Response was assessed by using RECIST (Response evaluation criteria in solid tumours) criteria and reported as complete response (CR) or partial response (PR) or progressive disease (PD) or stable disease (SD) CR: complete disappearance of all disease. PR: ≥30% reduction in the sum of the longest diameter of target lesions. Stable disease: change not meeting criteria for response or progression. Progressive disease: ≥20% increase in the smallest sum of the longest diameters of target lesions .

**Follow-up Protocol-**

Patients were seen monthly for first 6 months, 3monthly till 1 year, 6monthly till 3 years. Physical examination and complete blood profile was routinely done on each follow-up. chest x-ray, ECG, 2D Echo, CT Scan/MRI, Bone scan were done as per clinical indication.

**Outcome Protocol-**

Clinical outcome was assessed during follow up by clinical examination and chest x-ray, ECG , 2D Echo , CT Scan/MRI, as per clinical indication and categorized as no abnormality detected (NAD), recurrence, relapse or residual disease. Patients who has presented with disease within 6 months of treatment completion were termed residual tumor whereas patients in whom symptoms recurred after 6 months of treatment completion were relapse or recurrence.

**Statistical Analysis**

Data was compiled using MsExcel and analysed using IBM SPSS software version 20. Categorical data was expressed as frequency and percentage 30 whereas numerical data was expressed as mean and standard deviation. Odds ratio was calculated using univariate and multivariate analysis to assess the risk factors associated with recurrence.

**RESULT -**

The present study was carried in department of radiation oncology ,Gandhi Medical College, Bhopal Madhya Pradesh .The present study is retrospective, analytical study. The study was conducted on the patients of Breast Cancer presented to the institution in last ten years from 2010 to 2019.

Total number of patients visited during this period to hospital were 1303 of which 242 (18.5 %) patients did not come for regular follow up or took treatment at different hospitals and hence were considered loss to follow up or drop outs. Finally 1061 (81 % ) patients were treated and their outcome was considered for analysis in our study. - Average age was observed to be 47.36 years with SD of 11.66. Maximum number of the patients presented with IIIA stage( 44.2% ), maximum number of patients were having IDC (infiltrating ductal carcinoma ) or IVC ( invasive ductal carcinoma ) ( 84.07% ).

**Table 1. Distribution According To Base Line Variables**

Baseline variables	Number of patients	Percentage (%)	
Age (in years )	20-30	74	6.97
	31-40	289	27.23
	41-50	322	30.34
	51-60	248	23.37
	61-70	111	10.46
	71-80	17	1.60
	IIA	36	3.39
TNM staging	IIB	185	17.43
	IIIA	470	44.29
	IIIB	179	16.87
	IIIC	39	3.67
HPR of patients	IV	152	14.32
	IDC/IVC	892	84.07
	LC	169	15.92

Considering the hormonal receptors ER receptors were observed in majority of the patients with details are portrayed in table 2:

**Hormonal Receptors Found In Patients**

Hormonal receptor	No.of patients	Percentage (%)
ER	409	38.54
PR	305	28.74
HER2NEU	138	13.00
Unknown status	209	19.69

Considering the Family history of the patients majority of 96.98% of the patients were not having significant family history of carcinoma breast as depicted in table 3 :

**Table 3: Family History Of Breast Cancer**

Family history	Frequency	Percentage (%)
YES	32	3.01
NO	1029	96.98

Considering the total of 1061 patients nearly 154 patients were having metastasis at various sites out of which 62.9% Bone metastasis followed by 24.6% lung metastasis.

whose details are given in table 4 -A ,table 4-B

**Table 4 -a: Metastasis Occurrence In Patients Under Consideration**

Metastasis occurred	No. of patients	Percentage (%)
Yes	154	14.51
No	907	85.48

**Table 4 - B ; Metastatic Site Wise Distribution In The Patients ;**

Metastasis site	No. of patients	Percentage (%)
Bone	97	62.98
Lung	38	24.67
Brain	11	7.14
Liver	8	5.19

Considering the treatment received by the patients, Maximum number of patients were treated with Chemotherapy (84.8%) followed by surgery with nearly ( 76.3 %). Patients were treated as hormonal therapy with majority of Letrozole 27.5% , followed by Anastrozole 7.06% details of which are portrayed in table 5-A and table 5-B as:

**Table 5-a: Treatment Wise Distribution In The Patients : Chemo neoadjuvant Chemo adjuvant Surgery Hormonal Radiotherapy**

	Chemo neoadjuvant	Chemo adjuvant	Surgery	Hormonal
YES	900	403	810	435
798				
Percentage (%)	84.82	37.98	76.34	40.99
75.21				

**Table 5 -b: Hormonal Therapy Wise Distribution In The Patients:**

Hormonal therapy	No. of patients	Percentage (%)
Letrozole	292	27.52
Anastrozole	75	7.06
Tamoxifen	48	4.52
Unknown status	646	60.88

In view of the follow up of patients after the treatment; follow up was carried out at the interval of 3months, 6 months and 1year with average of 699.3 with SD of 169.99 patients have been followed for the mean time period of 6 months whose details are depicted in table 6.

**Table. 6: Follow Up Of The Patients After Treatment: FU 3MONTHS FU 6 MONTHS FU 12MONTHS**

Follow up	FU 3MONTHS	FU 6 MONTHS	FU 12MONTHS
Percentage (%)	81.33	72.57	43.8

Amongst the study population response to the treatment provided was assessed for which patients were monitored ----- PR (partial response ) CR(complete response ) and PD(progressive disease) . With majority of the patients were observed in PR with 46.5 % volume whose details are depicted in table 7.

**Table 7: Showing Population Response To The Treatment**

	CR	PR	Relapse	Recurrence	PD
Response	305	494	36	98	128
Percentage(%)	28.74	46.55	3.39	9.23	12.06

Considering the defaulters of the study nearly 18.57 % patients showed the negative response in follow up as depicted in table 8

**Table 8: Details Of Defaulters Amongst Patients**

Defaulters	No. of patients	Percentage (%)
YES	242	18.57
NO	1061	81.43

**DISCUSSION -**

The current study "A Ten-Year Retrospective Evaluation of Clinical and Treatment Outcomes of Carcinoma Breast " was conducted in the Department of Radiation Oncology, Gandhi Medical College and associated Hamidia Hospital Bhopal. The goal of the study was to assess the patient's demographics, disease characteristics, management, and outcome. Total number of patients visited during this period to hospital were 1303 of which 242 (18.57 %) patients did not come for regular follow up or took treatment at different hospitals and hence were considered loss to follow up or drop outs. Finally 1061 (81.1 % ) patients were treated and their outcome was considered for analysis in our study.

The average age of the patients in this study was 47.36 years with an SD of 11.66 (range 20 to 80 years), with majority of the participants being 41 to 50 years old (30.34 percent), followed by 31 to 40 years old (27.23%), which was found similar to a study conducted by Nalliah Manoharan et.al on the descriptive epidemiology of female breast cancer on 9,598 females, in which maximum cases[2,744 (28.6%)] were of a median age of 50 years. (19)

In present study, majority of patients belonged to locally advanced group [44.29 % of stage IIIA, 17.43 % of stage IIB, 16.87 % of stage IIIB and 3.6% of stage IIIC] whereas (14.33%) patients developed distant metastases during treatment [Stage IV]. Least number of cases were from early group [Stage IIA (3.3 %)] with no cases from stage I disease. The results were similar to the research conducted by Sunita et.al in Delhi where they retrospectively analysed 569 breast cancer cases diagnosed between 1989 and 2003, with Locally advanced cancers constituting the majority (78.6%) of cases. However early stage cases constituted around (13.6%) of total [(12.2%) of stage IIA and (1.2%) of stage I] followed by distant metastases group (7.69%), which was different from our study.(20)

Majority of patients enrolled in our study had histology of invasive (also known as infiltrating) ductal carcinoma (84%), followed by lobular carcinoma (15.9 %) , which is similar to the data published by American cancer society according to which around 70-80% are invasive or infiltrating ductal carcinoma followed by invasive lobular carcinoma. (21)

In our study, ER positivity was observed in 38.54% cases whereas PR positive was observed in 28.74% cases. Her2Neu receptor positivity was observed in only 13.0 % patients. Around 19.69% cases the hormonal status remained unknown due to financial constrains as these tests were not conducted in the hospital. only 3.29 % of total patients received trastuzumab therapy whereas majority of patients did not receive trastuzumab therapy due to the limited supply of trastuzumab. Amongst ER and PR receptor positive cases, Letrozole was the most common hormonal therapy prescribed in 27.52 % patients followed by Anastrozole in 7.06 % patients and lastly Tamoxifen in 4.52 % patients.

These results were in contrast to the study conducted by Onal C et.al, where the majority (75%) received tamoxifen followed by anastrozole in 22% patients.[22]

About (3.1%) of participants in present study had a positive family history whereas (96.9%) participants patients were devoid of any family history which is slightly lower to the data of (5%-10%) given by The American Cancer Society.

In our study, majority of patients (56.8%) were premenopausal; whereas only 43.1% were of

postmenopausal group. Menopausal status of the patient is essential to decide the line of management of patients with breast cancer, especially hormonal therapy. (23)

In present study 14.51% of patients developed distant metastasis with majority (62.98 %) to bones, (24.6 %) to lungs, (7.14 %) to brain and (5.19 %) to liver. A similar study was conducted by V Patanaphan at the University of Maryland Medical System where the most common first site of distant spread was bone (51%), followed by lung (17%), brain (16%), and liver (6%). The overall median survival time after metastasis was 12 months for bone and lung lesions, three months for brain lesions, and only one month for liver metastasis. (24)

About 84.8 % of the enrolled patients in our study received neoadjuvant chemotherapy whereas 15.2 % patients did not received it , as they were post operative or with metastatic disease at initial presentation. Adjuvant chemo therapy was given in 37.9 % of patients. Majority of patients received CAF regimen (72.76%), which was followed by TAC regimen in (14.13%), followed by CEF regimen in (5.93%), followed by AC + TAXOL regimen in (2.5%). About 4.77 % patients received other regimes of chemotherapy. Surgical intervention was done in about (76.3%) of patients with majority of patients undergoing Modified Radical Mastectomy (MRM). Around 75 % of patients received radiotherapy to the affected breast emphasizing its importance in management in breast cancers. Around 40 % of patients received hormonal therapy in one or the other form. Patients were treated as hormonal therapy with majority of Letrozole 27.5% , followed by Anastrozole 7.06% .

Anthracycline-based regimens provide a small but significant benefit over cyclophosphamide, methotrexate, and fluorouracil regimens (25). Similar study conducted by Chau T. Dang; Gabriella M. D'Andrea in which develop an "ideal" adjuvant chemotherapy regimen, we chose FEC × 6 followed by weekly paclitaxel alternating with docetaxel × 18. Thus, this regimen included 6 cycles of an anthracycline-based regimen and 18 weeks of taxane therapy and, if feasible, could not be criticized as compromising (underdelivering) chemotherapy treatment. Unfortunately, as designed this regimen was not feasible. Only (39%) patients completed the study as planned, and the study was closed early because (12%) patients experienced grade 4 pericardial and grade 3 pleural effusions, requiring surgical treatment. With extensive evaluation, it was felt that the pericardial/pleural effusions were most likely due to alternating schedule of taxanes (26).

The maximum follow up of patients in 3 month after treatment is approx 81 % in present study followed by 72 % in 6 month and 44 % in 12 month . follow up was carried out at the interval of 3months, 6 months and 1year with average of 699.3 with SD of 169.99 patients have been followed for the mean time period of 6 months.

Response evaluation was done on the basis of RECIST criteria. Majority (47%) of the patients showed partial response (PR) , followed by complete response (CR) in around (28.74%) patients. About (12%) of patients did not responded to treatment and were classified as having progressive disease (PD). Of the total patients around (9.2%) of patients developed recurrence whereas around (3.3%) patients relapsed during the course of disease.

## CONCLUSION -

Breast cancer is the most common malignancies prevalent in India in female and are major public health burden. There are wide variations in risk factors, geographical, and demographic characteristics. Incidence of breast cancer are increasing because of lack of awareness, increasing with age . The decrease in incidence rate that occurs in women 80 years

of age and older may reflect lower rates of screening . Widely spread educational campaigns against determinant factors should be introduced in order to reduce incidence rates. Majority of the patients present at locally advanced stage hence neoadjuvant chemotherapy plays an important role in downstaging the tumour. Standard follow-up of patients treated for breast cancer is based on regular follow-up visits, with frequency decreasing in consecutive years.

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