J. Pharm. Res. 2023;22(2):93–97

Print ISSN: 0973-7200
Online ISSN: 2454-8405

Journal of Pharmaceutical Research

Research Article

A Study on Prognostic Factors in Management of Breast Carcinoma in A Tertiary Care Hospital

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ARTICLE INFO

Article history:
Received 05.07.2023
Accepted 10.09.2023
Published 09.10.2023

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https://doi.org/10.18579/jopcr/v22.2.23.42

ABSTRACT

Breast cancer is the most common malignant tumor and leading cause of death in women worldwide. It accounts for 15% of all cancer deaths According to World Health Organisation (WHO), approximately 70% of breast malignancies occur in women with unknown risk factorsThe prognostic factor can be defined as a measurable variable which correlates with natural history of the disease. The most significant factor which influences prognosis in breast cancer is axillary lymph node involvement, which is usually assessed at time of surgery using sentinel lymph node biopsy or axillary lymph node dissection. The number of lymph nodal involvement is also significant. Involvement of 1-3 lymph nodes carry better prognosis than 4-9 and more than 9 lymph nodes involvement. Size of the tumour has long been recognized as a prognostic factor and as predictor of axillary node status, with larger tumours being associated with a bad prognosis and an increased incidence of nodal metastasis. This study is conducted in Department of General Surgery, SVRRGGH, Sri Venkateswara Medical College, Tirupati for a period of more than one and half year after getting approval from Institutional Ethical Committee on March 2021. A prospective study of 50 patients who fulfilled Inclusion Criteria is taken into consideration to know how prognostic factors like tumor size & grade, axillary lymphnode involvement are influencing the prognosis and management of breast carcinoma. Patients who took part in the study were from 28-68 years of age. Majority of people were in the age group of 46-55 years (38%). Increasing age, involvement of axillary lymph nodes, tumors with larger size and higher grade, and lymphovascular invasions are all associated with worse prognosis

Keywords: Estrogen Receptor; Progesterone Receptor; Locally Advanced Breast Carcinoma

INTRODUCTION

Breast cancer is most common malignant tumour and leading cause of death in women worldwide[1]. It accounts for 15% of all cancer deaths[2]. According to World Health Organisation (WHO), approximately 70% of breast malignancies occur in women with unknown risk factors. Only about 5% of breast malignancies are inherited. Number of global cancer deaths is projected to increase by 45% from 2007- 2030 (from 7.9 million to 11.5 million deaths), influenced in part by an increasing and ageing global population[3]. Women with breast cancer have relative survival rates of 96%, 79 %,67% and 60% for 1, 5, 10 and 15 years respectively[4]. Various protocols are in use for the assessment of prognosis and also to assist further management of these cases.

The prognostic factor can be defined as a measurable variable which correlates with natural history of the disease. The most significant factor which influences prognosis in breast cancer is axillary lymph node involvement, which is usually assessed at time of surgery using sentinel lymph node biopsy or axillary lymph node dissection. The number of lymph nodal involvement is also significant. Involvement of 1-3 lymph nodes carry better prognosis than 4-9 and more than 9 lymph nodes involvement. Size of the tumour has long been recognized as a prognostic factor and as predictor of axillary node status, with larger tumours being associated with a bad prognosis and an increased incidence of nodal metastasis. Other prognostic factors include lymphovascular

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invasion, age of the patient and histological tumour grade. Few histologic variants of breast carcinoma are associated with a favourable prognosis like tubular, colloid (mucinous) and papillary carcinoma. Proliferation rate of tumour is defined by mitotic count which is of prognostic importance. Breast carcinoma cells may contain receptors or binding sites for the hormones estrogen and progesterone[5]. Cells containing these receptors are known as hormone receptor-positive cells. If cells lack these receptors, they are called hormone receptor negative cells. About 75% of breast malignancies are estrogen receptor positive (ER positive, or ER+). About 65% of ER-positive breast malignancies are progesterone receptor-positive (PR-positive, or PR+). All cases of breast malignancies are assessed for ER/PR status using immunochemistry which has prognostic and predictive value. The literature includes various studies explaining association between the presence of estrogen & progesterone receptor and other indicators of good prognosis like small tumour size, low histological grade, and low mitotic activity(5). It is also a significant factor for the likelihood of benefit from adjuvant hormonal therapy like aromatase inhibitors (Anastrozole, letrozole) and Tamoxifen, an oral selective estrogen receptor modulator[6,7].

MATERIAL & METHODS

This study is conducted in Department of General Surgery, SVRRGGH, Sri Venkateswara Medical College, Tirupati for a period of more than one and half year after getting approval from Institutional Ethical Committee on March 2021. A prospective study of 50 patients who fulfilled Inclusion Criteria are taken into consideration to know how prognostic factors like tumor size & grade, axillary lymphnode involvement are influencing the prognosis and management of breast carcinoma.

1. I**nclusion criteria:** Female patients above age 18 years presenting to General Surgery OPD with breast carcinoma
2. **Exclusion Criteria:** Patient with benign breast diseases., inflammatory breast carcinoma. , systemic metastases & inoperable breast cancer.

Study methods

Patients satisfying inclusion criteria and exclusion criteria were selected. Demographic data collection, detailed clinical history taking & a careful Clinical examination conduction were accomplished. Written consent was taken from every patient included in study. Patient were admitted, investigated and evaluated for assessment of general condition and specific investigative workup to establish diagnosis and to rule out any other pathologies of breast.

RESULTS & DISCUSSION

- **Age:** Patients who took part in the study were from 28-68 years of age. Majority of people were in the age group of 46-55 years (38%), followed by 36-45 years (30%) and above 55 years. Mean age of patients in this study is 48.9 years. Among 50 cases 6 cases showed recurrence. 3 patients are in above 55 years age group and 2 are from 36-45 years group and remaining one from 46-55 years group.
- **Clinical findings:** Out of 50 patients, 45 patients presented with lump, 4 patients with ulcer, one with pain over the lump. None had the complaints of back-ache, bone pains, respiratory complaints, abdominal complaints.
- **Duration of complaints:** Among 50 cases 20 presented with in 2-4 months of duration. 26 cases presented with 5-7 months of duration. 2 cases presented with history of 8-10 months and remaining 2 presented with more than 10 months history. Mean duration of the presentation in this group is 5.38 months.
- **Age at menarche:** In the study conducted by taking detailed history out of 50 cases. 22 attained menarche at their 13 years age, 19 attained at 14 years age and 9 attained at12 years of age. Mean age of menarche is 13.2 years.
- **Breasst feeding:** Among 50 cases 47 women breastfed their babies while remaining 3 did not. Age at menopause: While observing the menstrual history of 50 cases 24 completed their menopause and remaining 26 are still having their menstrual cycles.
- **Tumour size and nodal status by TNM staging:** While observing the tumour size in the study group 6% patients presented with T1. 34% patients presented with T@/ 46% patients presented with T3. 14% patients with T4B stage. While observing the lymphnode status 96% of patients showed node positive status 4% showed node negative status. Percentage of recurrence is 12% among 50 cases. Percentage of recurrence among node positive cases is 12.5%.
- **TNM staging:** 40% of patients in study group were in stage III A. 34% were in stage II B. 18% were in stage III B. 6% were in stage II A. remaining 2% were in stage I

Table 1: TNM staging

TNM Staging	No. Patients	%	Recurrence
Stage 1	1	2.0	0
Stage II A	3	6.0	1
Stage II B	17	34.0	1
Stage III A	20	40.0	2
Stage III B	9	18.0	2
Total	50	100.0	6

- **Stage of disease:** 42% of patients in study group are in EBC. 58% were in LABC. 9.52% patients showed recurrence in EBC group where as 13.79% patients in LABC group.

Table 2: Stage of disease

EBC/LABC	No. Patients	%	Recurrence
EBC	21	42.0	2
LABC	29	58.0	4
Total	50	100.0	6

- **Lymphatic invasion:** On HPE lymphatic invasion was found in 38 patients and not found in 12 patients. 5 cases of recurrence were noted out of 38 patients with lymphatic invasion and 1 out of 12 patients without lymphatic invasion. Percentage of recurrence in the patients with lymphatic invasion is 13.15% and in the patients without lymphatic invasion 8.3%.
- **Vascular invasion:** Vascular invasion was found in 16 patients out of 50. Six cases of recurrence noted out of which 4 cases from patients with vascular invasion and 2 from patients without invasion. Percentage of recurrence in the patients with vascular invasion is 25% and percentage of recurrence in the patients without vascular invasion is 5.8%. Recurrence is more common in patients with vascular invasion which indicates poor prognosis.
- **Histological Grading:** Modified Bloom Richardsons (MBR): Out of 50 patients based on HPE 24 patients are in Grade II Grade I and 9 are in Grade III. Among 6 recurrent cases 4 are from patients with Grade III, 2 are from the patients with Grade II. Percentage of recurrence is 44.4% from the patients with grade III. 8.3% is from the patients with grade II

Table 3: Histologic Grading

MBR	No. Patients	%	Recurrence
Grade I	17	34	0
Grade II	24	48	2
Grade III	9	18	4
Total	50	100	6

- **Histological types of Breast Cancer:** Most common histological type of breast carcinoma was invasive ductal carcinoma (NOS) type. 40 out of 50 patients had IDC-NOS. Next followed by IDC+ILC and IDC-Comedone. Recurrence occurred in 6 out of 50 among which 3 are from IDC-NOS and 1 from IDC-Comedone, 1 from medullary and 1 from NHL-undifferentiated.

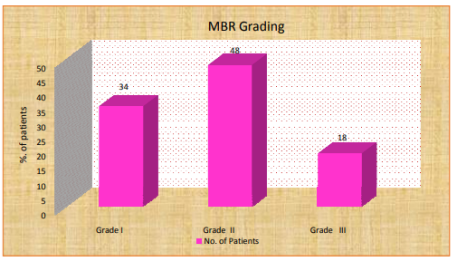

Fig. 1: MBR grading

Table 4: Histological types

Histological	No. Patients	%	Recurrence
IDC ILC	3	6	0
IDC-Come done	3	6	1
IDC-NOS	40	80	3
Medullary	2	4	1
NEC, Undifferentiated	2	4	1
Total	50	100	6

DISCUSSION

- **Age:** Patients who took part in this study were from 28 to 68 years of age. Majority of people were in age group of 46-55yrs (38 per cent) followed by 36 – 45 years (30 per cent) and aged above 55. The mean age of the patients in the study is 48.9 years which is much lower than 62yrs reported in study by Adedayo A onitilo et al.

Table 5: Comparison of mean age at presentation

Raina V et al	2005	47 yrs
Adedayo Aonitilo et al	2009	62.7 yrs
Gulam Nabi Sofi et al	2012	48.2 yrs
Manilal B et al breast	2016	35.1 yrs
Divyasreee et al clinicl	2018	34 yrs
Rupporn et al pak	2019	61.7 yrs
Present study	2021-2022	48.9 yrs

- **Clinical presentation:** Out of 50 patients in this study, 45 patients presented with lump in the breast, 4 patients with ulcer over the breast, 1 patient with pain over lump. None of the patients included in this study presented with nipple discharge. None of these 40 patients had the complaints of symptoms due to metastases like backache, bone pains, respiratory complaints and abdominal complaints. In this study conducted by Divyasree et al, out of 185 cases, 170 cases presented with a lump in breast and of the remaining 15 cases, 5 patients presented with nipple discharge alone while other 10 cases with both lump and nipple discharge. Most of the patients presented with lump,

associated compliant was pain. These results were similar to my study.

- **Duration of complaints:** Among 50 patients included in the present study, 20 patients presented with in 2-4 months of duration of symptoms. 26 cases presented with 5-7months of duration of symptomatology. 2 cases presented with history of 8-10 months and remaining 2 patients presented with more than 10 months of history. Mean duration of the presentation of the patients in this group is 5.38mnths.
- **Age at Menarche:** Out of 50 patients taken in this study, 22 patients have attained menarche at 13years of age, 19 patients attained at 14years age, 9 patients attained at 12 years of age. Mean age of menarche of patients in my study is 13.2years.
- **Breast feeding:** Among 50 cases recruited in this current study, 47 women have breastfed their babies exclusively for 1 year, while remaining 3 patients have not breast fed their babies.
- **Age at Menopause:** Elaborate history was elucidated from all the patients participated in the study. While observing the menstrual history of 50 cases, 24 completed their menopause and remaining 26 are still having their menstrual cycles.
- **Comparison of axillary lymphnodal status:** While observing the axillary lymph nodal status in my study, 96% of patients showed node positive axillary lymph node status. 4% of patients showed node negative status in the axilla.

Table 6: Comparison of axillary lymphnodal status

Lakmini K B Mudduwa et al	2009	57.7% positive
Adedayo A Onitilo et al	2009	31% Positive
Gulam Nabi Sofi et al	2012	65.2% Positive
Divyasree et al	2018	41.1% Positive
Rupporn et al	2019	71% Positive
Present Study	2021-2022	96% Positive

- **Comparison of tumor size:** By analysing the results from current study, ● 6 per cent of patients presented with T1 lesion (less than 2cm). ● 34 per cent of patients presented with T2 lesion (2 – 5 cm). ● 46% of patients with T3 lesion (more than 5 cm). ● 14 per cent of patients presented with T4 lesion (any size with one of following - i. skin involvement, ii. Chest wall involvement, iii. Both, iv. Inflammatory breast cancer). Most of patients presented with T3 lesion followed by T2 lesion in present study. In this study, six cases of loco regional recurrence were found on follow up. Among those three patients were T3 lesion, two cases were T4b lesion and the remaining one patient with T2 lesion. The patients who were recruited in my study presented with large sized lumps probably due to poor socio economic status, un awareness and lack of effective screening methods. As the tumour size increases, recurrence rate increases and prognosis also becomes poor with increasing in tumour size.

Table 7: Comparison of tumour size

Lakmini K B Mudduwa et al	2009	2-5cm (74%)
Raina V et al	2005	2-5cm (86.4%)
Adedayo A Onitilo et al	2009	<2cm (71.4%)
Gulam Nabi Sofi et al	2012	2-5cm (65.1%)
Divyasree et al	2018	2-5cm (88.8%)
Rupporn et al	2019	2-5cm (92.8%)
Present Study	2021-2022	96% Positive

- **Comparison of Histology:** Most common histologic type of breast carcinoma was Invasive Ductal carcinoma (NOS) type in the current study. Forty patients out of 50 patients in my study had Invasive ductal carcinoma(IDC-NOS). It is followed by Invasive ductal carcinoma, intra lobular carcinoma and Intraductal carcinoma-comedone. Among 6 cases of recurrence which were observed on follow up in my study, three cases were with Intra ductal carcinoma -not otherwise specified type, one case of Intraductal carcinoma-comedone, one case of medullary type and other case of NHL-Undifferentiated.

Table 8: comparison of Histology

Adedayo A Onitilo et al	2009	IDC – NOS (72.7%)
Gulam Nabi Sofi et al	2012	IDC – NOS (80.3%)
Manilal B et al	2016	IDC – NOS (93.5%)
Divyasree et al	2018	IDC – NOS (79.41%)
Present Study	2021-2022	IDC – NOS (80%)

- **Tumor Grading:** In our study, patients presented with Grade II tumours (48 per cent) were common followed by grade I (34 per cent) and then by grade III (18 per cent). But above results are in contrast to the reported observations in studies done in developed countries where well differentiated breast malignancies are more common when compared to poorly differentiated because of use of routine screening mammography which has led to detection of very early lesions.

CONCLUSION

Outstanding advances in breast cancer diagnosis and treatment has been made in recent years, allowing for earlier disease identification and the creation of more efficient multimodality therapies. With this progress, women living

Table 9: Tumor Grading

Lakmini K B Mudduwa et al	2009	I-14.6%. II-36.4%, III-49%
T B Pathak et al	2011	I-20%. II-59%, III-21%
Adedayo A Onitilo et al	2009	I-21.2%. II-38.4%, III-35.9%
Gulam Nabi Sofi et al	2012	I-7.6%. II-52.1%, III-40.3%
Present Study	2021-2022	I-34%. II-48%, III-18%

with breast carcinoma can lead a better quality of life and a notable drop in breast cancer deaths. Classical factors that affect the prognosis and management of breast carcinoma include the histological type and grade, size of tumour, status of lymph nodes, status of hormone receptors - ER and PR. This study is an attempt that was made to assess the prognostic factors and their role in management of breast carcinoma. In present study, all cases have received surgical care before being transferred to a higher level facility for adjuvant chemotherapy and radiotherapy for loco regionally advanced cancer. Increasing age, involvement of axillary lymphnodes, tumors with larger size and higher grade, lymphovascular invasionsare all associated with worse prognosis.

REFERENCES

1. Parkin DM, Bray F, Ferlay J, Pisani P. Estimating the world cancer burden: Globocan 2000. *Int J Cancer*. 2001;94(2):153–156. Available from: https://doi.org/10.1002/ijc.1440.
2. Jemal A, Thomas A, Murray T, Thun M. Cancer statistics, 2002. *CA Cancer J Clin*. 2002;52(1):23–47. Available from: https://doi.org/10.3322/canjclin.52.1.23.
3. Woodsen RVD. The Problem- Prevalence of breast cancer . 2010.
4. Wingo PA, Ries LA, Parker SL, Jr CWH. Long-term cancer patient survival in the united states. *Cancer Epidemol Biomarkers*. 1998;7(4):271–282. Available from: https://pubmed.ncbi.nlm.nih.gov/9568781/.
5. Lester SC, Kumar V, Abbas AK, Fausto N, Aster JC. The Breast. In: Kumar V, Abbas AK, Fausto N, Aster JC, editors. Robbins and Cotran Pathologic Basis of Disease. Saunders. 2010;p. 1065–1087.
6. Fisher B, Jeong JH, Bryant J, Anderson S, Dignam J, Fisher ER, et al. Treatment of lymph-node-negative, oestrogen-receptor-positive breast cancer: long-term findings from National Surgical Adjuvant Breast and Bowel Project randomised clinical trials. *The Lancet*. 2004;364(9437):858–868. Available from: https://doi.org/10.1016/s0140-6736(04)16981-x.
7. Group E. Tamoxifen for early breast cancer: an overview of the randomised trials. Early Breast Cancer Trialists' Collaborative Group. *Lancet*. 1998;351(9114):1451–1467. Available from: https://pubmed.ncbi.nlm.nih.gov/9605801/.