

# Correlation of Various Prognostic Factors in Breast Cancer

Dr Navneet Kumar\*, Dr Sumedha Mukherjee\*\*

\* V S Hospital, Ahmedabad

\*\* Dr BC Roy Institute of Pediatric Sciences, Kolkata

**Abstract- Background:** Prognostic factors of breast cancer not only act as a guide to overall prognosis but also determine the need for adjuvant therapy. These factors are interrelated and hormone receptor status is an important determinant of prognosis of ca breast. **Objective:** The aim of this study was to correlate the various prognostic factors in breast cancer. Tumor size (T), nodal status (N), grade of the tumour and ER PR status were taken as prognostic factors. **Materials and Methods:** Mastectomy Specimen of fifty patients of carcinoma breast were studied to ascertain its size, status of margin, histology of the tumor, lymph node metastasis to determine modified Richards Bloomson's (MRB) score and Nottingham Prognostic Index (NPI). The Estrogen and progesterone receptor status was identified, data was analysed statistically by using Chi-square test and conclusion was drawn. **Results:** Most of the patients were 40-60 yr of age group, however most were postmenopausal and 40% of the patients had no metastasis in axillary lymph nodes. Tumour was hormone receptor positive in two third of the patients. Hormone receptor positivity decreased with increase in size of the tumour, axillary lymph node positivity and grade of the tumour. Hormone receptor positivity increased as the age advances and positivity was more in postmenopausal as compared to premenopausal. Axillary lymph node involvement were increased with size of the tumour also increased size of the tumour leads to increase in the grading of the tumour. **Conclusion:** More number of patients are presenting in early stage as majority of patients have operable breast cancer. Most of the patients were between 40-60 yr of age which suggest shift towards younger age groups as compared to the traditional presentation of older age. Tumour was hormone receptor positive in two third of the patients. Small size, low grade and tumours without axillary lymph node metastasis have more chances of receptor positivity.

**Index Terms-** prognostic factors, Nottingham prognostic index, er pr status.

## I. INTRODUCTION

World-over carcinoma breast is the most frequent type of cancer among females. In India, it is the second most prevalent cancer among females after carcinoma of cervix, not only this but it is leading cause of cancer death in women aged 40 to 44 years, and second leading cause of cancer death for women overall.

There has been slight decline in breast cancer mortality overall, which can be attributed both to success of early detection

programs and to advances in treatment, particularly development in systemic therapy.<sup>1</sup>

The current management of primary breast cancer involve the need for prognostication and the optimal selection of therapy. Estrogen receptor status has been clearly shown to be a predictive factor for hormonal therapy, in both the adjuvant and metastatic disease settings. Prognostication is especially important in identifying patients whose prognosis are so favorable that adjuvant systemic therapy is unnecessary. Prognostic factors can also be useful in identifying patients whose prognosis with conventional treatment are so poor as to warrant consideration of more aggressive investigational therapies.<sup>1</sup>

Prognostic factor not only act as a guide to overall prognosis but they may also determine need for adjuvant treatment. Clinical and pathological factors important and useful in prognostication are axillary lymph node status, stage of disease, size of primary tumor, histological grade, oestrogen and progesterone receptor status, lymphatic and vascular invasion, DNA flow cytometry, S-phase fraction, HER-2/new oncogene, cathepsin-D and epidermal growth factor receptor.<sup>2</sup>

The most established prognostic factor is the number of positive axillary lymph node based on at least a level I or II axillary dissection and a detailed histologic evaluation.<sup>1</sup>

Overall 10-year survival is reduced from 75% for node-negative patients to 25-30% for node-positive patients. The prognosis is also related to the number and level of locoregional lymph nodes involved. The greater the number of nodes involved, the poorer the prognosis.<sup>4</sup>

Tumor size, one of the first prognostic variables accurately quantified, is also a valuable prognostic factor. Tumor size correlates with the number of histologically involved nodes, but has independent prognostic significance. The size of the primary tumor is strongly correlated with lymph node metastasis.<sup>6</sup> Axillary nodes are involved in 45% of patients when the tumor is equal to or less than 1cm and is 60% when the tumor size is greater than 5cm.

Tumor grade is commonly provided on pathology reports and several investigators have demonstrated that it is an important prognostic factor in individual series. The use of tumor grade, however, has been limited by poor reproduction.<sup>8</sup>

Among clinical factors, young patient age has been reported to be an adverse prognosis. Women who are younger than 50 years of age at the time of diagnosis have the best prognosis. Relative survival declines after the age of 50 years and is particularly low in older women.<sup>9</sup>

Oestrogen receptors and progesterone receptors were used primarily as predictive factors for hormone responsiveness in

metastatic breast cancer.<sup>16</sup> Subsequently, they were also shown to be determinants of prognosis in early disease.<sup>17</sup> The presence of oestrogen receptors correlates inversely with certain histological features such as histological and nuclear grade, tumour proliferative index, lymphocytic infiltration and tumor necrosis; while it correlates positively with elastosis.<sup>18</sup> Oestrogen receptor positivity is a better predictor of overall than disease free survival and this has been interpreted as suggesting that the prognostic influence of oestrogen receptors is largely related to better survival of oestrogen receptor positive patients after relapse.<sup>19,20</sup> In addition to being a predictive factor for hormone responsiveness in metastatic breast cancer estrogen receptor status has been shown to predict benefit from tamoxifen in both pre and postmenopausal women in the adjuvant setting.<sup>21</sup>

Oestrogen receptor and prognosis : Most studies agree that expression of ER is a marker of favourable prognosis and patients have an overall survival advantage. There is a positive correlation between tumor differentiation, absence of lymph node metastases and positive ER status. Size and type of tumor are also important; smaller tumours and certain histological types, such as lobular carcinoma, are more likely to be receptor positive. ER levels are usually higher and incidences are usually more frequent in postmenopausal patients.<sup>22</sup>

## II. MATERIALS AND METHODS

The study was conducted on 50 patients of carcinoma breast. Cases of carcinoma breast diagnosed by clinical examination and confirmed by fine needle aspiration and cytology (FNAC) and histopathological examination were included in the study. Routine and special investigations such as USG abdomen and pelvis, X-ray chest, CT scan of chest / abdomen / head were conducted wherever required to detect distant metastasis. After initial tissue diagnosis on FNAC / biopsy and clinical staging, patients were taken up for surgery. The specimens were sent in buffered formal saline for detailed gross and microscopic examination to ascertain its size, status of margin, histology of the tumor, lymphnode metastasis etc. to determine modified Richards Bloomson's (MRB) score and Nottingham Prognostic Index (NPI).

MRB grade was obtained by adding up the scores for tubule formation, nuclear pleomorphism and mitotic count. Each of which was given 1, 2 or 3 points. This resulted in a total score of between 3 and 9. The final grading was given as below

1. 3 to 5 points – grade I
2. 6 to 7 points– grade II
3. 8 to 9 points–grade III.

The Nottingham Prognostic Index was calculated by using three prognostic factors – lymph node stage, tumor size and histologic grade. Index formula which used was

$$NPI = [\text{Size (cm)} \times 0.2] + [\text{Lymph node stage (1-3)}] + [\text{grade (1-3)}].$$

According to NPI three prognostic groups were identified ; a good group with scores of less than 3.4 ; a moderate group with scores of 3.4 – 5.4; a poor group with score of over 5.4. The sections of the tumors were stained by standard

immunohistochemical stains for Estrogen and progesterone receptor status. Estrogen receptor and progesterone receptor status of the specimens were obtained. All relevant data thus obtained was put into chart and observation tables were made. Data was analysed statically by using Chi-square test and conclusion was drawn.

## III. RESULT

Out of fifty cases 20(40%) were of 50-59 years , 19(38%) were 40-49 years,4(8%)were of 30-39 years and 7(14%) were of >60 years age group. Out of fifty 41(82%) were postmenopausal and 9(18%) were premenopausal. Receptor status showed 31(62%) were ER PR +,6(12%) were ER PR –ve,3(6%) were ER+PR –ve and 10(20%) were ER-PR+ve. Histopathological grading of the tumor showed 41(82%) were grade II,5(10%) were grade I and 4(8%) were grade III. Correlation of hormone receptor status with tumor size in showed that in T1 stage out of 6 patients, 5(83%) were ER PR +ve ,in stage T2 out of 38 patients 24(63%) were ER PR +ve and 4 out of 38 (10%) were ER PR –ve. In the stage T3 out of 5 patients 2(40%) were ER PR +ve and 1 out of 5(20%) was ER PR –ve. Out of fifty 26(52%) were of N1 stage,4(8%) were stage N2 and 20(40%) were without axillary lymph node involvement. Correlation of lymph node status and size of the tumors showed that 26 out of 50(52%) patients were of N1. T2, T3 and T4 shows increase in lymph node positivity as three out five(60%) in the T3 was in N2 lymph node status, whereas all of T4 was of N2 lymph node status. Correlation of hormone receptor status and axillary lymph node status showed that among the ER PR+ve group, 45.16% of patients had no nodal involvement, 51.61% was of N<sub>1</sub> lymph node status and only 3.22% was of N<sub>2</sub>. While in ER PR-ve group 83.33% of patients had N<sub>1</sub> nodal involvement and 16.66% had N<sub>2</sub> lymph node status. Histopathological grading and hormone receptor status correlation showed that out of 41 grade II patients 24(58%) were ER PR +ve ,5 out of 41(12%) were ER PR –ve. In grade III ,2 out of 4 (50%) were ER PR +ve ,1 out of 4(25%) were ER PR –ve. Whereas all the 5 patients of grade I were hormone receptor positive. Correlation of histopathological grading and size of the tumour showed that in grade II most were of T<sub>2</sub> size 33 out of 41(81%),5(12%) were of either T3 or T4. In the grade III 3 out of 4 (75%) were of size T2 and 1 out of 4(25%) was of T2. In grade I out of 5 patients 3(60%) were of T1 and the rest 2 out of 5 (40%) were of T2 size. Lymph nodes status and histopathological grading correlation showed that out of 41 grade II tumours 24 was of N1 lymph node status 16 was of NO and the rest 1 was of N2 status. In the grade III out of four three were of N2 lymph node status one was of N1 and there was none without lymphatic involvement.

## IV. DISCUSSION

Present study of breast carcinoma showed 40% belonged to 50-59 year age group, 38% to 40-49 year age group ,8 % to 30-39 year age group and 1.4% to >60 year of age group . These findings showed that most (78%) of the breast cancer in our study was of the age group 40-60 yr and of early stages. These results are suggestive of changing pattern of indian society in

which there is increase awareness for carcinoma breast. 68.29% of postmenopausal patients were ER PR+ and 33.33% of premenopausal patients were ER PR+,menopausal status increases hormone receptor positivity. Hormone receptor status correlation with tumor size in breast cancer, showed that in T1 stage out of 6 patients, 5(83%) were ER PR +ve ,in stage T2 out of 38 patients 24(63%) were ER PR +ve and 4 out of 38 (10%) were ER PR –ve. In the stage T3 out of 5 patients 2(40%) were ER PR +ve and 1 out of 5(20%) was ER PR –ve. It showed that ER PR+ivity is decreased with increase in size of the tumour and hormone receptor negativity was increased with tumour size.

Hormone receptor correlation with axillary lymph node status showed that among the ER PR+ve group, 45.16% of patients had no nodal involvement, 51.61% was of N<sub>1</sub> lymph node status and only 3.22% was of N<sub>2</sub>. While in ER PR-ve group 83.33% of patients had N<sub>1</sub> nodal involvement and 16.66% had N<sub>2</sub> lymph node status. This showed that lymph node involvement is more in hormone receptor negative tumour as compared to hormone receptor positive tumour.

When histopathological grading and hormone receptor status was correlated ,it was found that out of 41 grade II patients 24(58%) were ER PR +ve ,5 out of 41(12%) were ER PR –ve.In

grade III ,2 out of 4 (50%) were ER PR +ve ,1 out of 4(25%) were ER PR –ve.Whereas all the 5 patients of grade I were hormone receptor positive.These findings suggest that as the grading of the tumour is increasing its hormone receptor positivity is decreasing while hormone receptor negativity is increasing.

When lymph node status and size of the tumors were correlated it was found that 26 out of 50(52%) patients were of N<sub>1</sub>. T<sub>2</sub>, T<sub>3</sub> and T<sub>4</sub> shows increase in lymph node positivity as three out five(60%) in the T<sub>3</sub> was in N<sub>2</sub> lymph node status, whereas all of T<sub>4</sub> was of N<sub>2</sub> lymph node status.Therefore axillary lymph node involvement were increased as the tumour size was increased.When histopathological grading was correlated with size of the tumour,it showed that most of the patients of ca breast were of grade II, 41 out of 50(82%),only five was of grade I and four was of grade III. In the grade II most were of T<sub>2</sub> size 33 out of 41(81%),5(12%) were of either T<sub>3</sub> or T<sub>4</sub>.In the grade III 3 out of 4 (75%) were of size T<sub>2</sub> and 1 out of 4(25%) was of T<sub>2</sub>.In grade I out of 5 patients 3(60%) were of T<sub>1</sub> and the rest 2 out of 5 (40%) were of T<sub>2</sub> size.Therefore as the size of the tumours were increased its grade were also increased.

#### Relationship between ER PR status and lymph node involvement in breast cancer patients

ER/PR Status	LYMPH NODE								Total No.	
	N <sub>0</sub>		N <sub>1</sub>		N <sub>2</sub>		N <sub>3</sub>		No.	%
	No.	%	No.	%	No.	%	No.	%		
ER+ve PR+ve	14	45.16	16	51.61	01	3.22			31	62
ER+ve PR-ve			2	66.66	01	33.33			3	06
ER-ve PR+ve	06	60	03	30	01	10			10	20
ER-ve PR-ve			05	83.33	01	16.66			6	12
Total	20	40	26	52	04	8			50	100

#### Relationship between histopathological grading and ER PR status in breast cancer patients

S.No.	ER PR Status	Histopathological Grade						Total No.	
		Grade – I		Grade – II		Grade – III		No.	%
		No.	%	No.	%	No.	%		
1	ER+ve PR+ve	05	16.12	24	77.41	02	6.4	31	62
2	ER+ve PR-ve			02	66.66	01	33.33	3	06
3	ER-ve PR+ve			10	100			10	20
4	ER-ve PR-ve			05	83.33	01	16.66	6	12
	Total	05	10	41	82	04	8	50	100

#### REFERENCES

- Devita VT, Hellman S, Rosenberg A. In: Cancer-principles and practice of oncology 6<sup>th</sup> edn. William and Wilkins. Philadelphia 2001. p. 1687.
- Stewart B, Kleihues P. World Cancer Report. IARC press Lyon. 2003. p. 191.
- Gloeckler RLA, Henson DE, Harras A. Survival from breast cancer according to tumor size and nodal status. Surg Oncol Clin N Am 1994;3:35-53.
- Elston CW, Greshan GA, Rao GS. The cancer research campaign trial for early breast cancer pathological aspects.Br J Cancer 1982;45:655-69
- Christopher DM, Fletcher R. Diagnostic Histopathology of Tumors, second edition. Churchill Livingstone London 2000;2:902.

- Knight WA, Livingston RB, Gregory EJ, McGuire WL. Estrogen receptor as an independent prognostic factor for early recurrence in breast cancer Cancer Res 1977;37:4669-71.
- Scarff RW, Torloni H. Histological typing of breast tumors. International histological classification of tumours,. World Health Organization, Geneva 1968;2:13-20.
- Bloom, H.J. and Richardson W.W. Histological grading and prognosis in breast cancer. Br. J. Cancer, 1957;11: 359-377.
- Elston, C.W. The assessment of histological differentiation in breast cancer. Aust N Z J Surg 1984; 54, 11-5.
- Elston CW, Ellis IO. Pathological prognostic factors in breast cancer. I. The value of histological grade in breast cancer: experience from a large study with long-term follow-up. Histopathology1991;19:403-10.

- [11] Dalton LW, Pinder SE, Elston CE, Ellis IO, Page DL, Dupont WD, et al. Histologic grading of breast cancer: linkage of patient outcome with level of pathologist agreement. *Mod Pathol* 2000;13:730-5.
- [12] Le Doussal V, Tubiana-Hulin M, Friedman S, Hacene K, Spyrtos F, Brunet M. Prognostic value of histologic grade nuclear components of Scarff-Bloom-Richardson (SBR). An improved score modification based on a multivariate analysis of 1262 invasive ductal breast carcinomas. *Cancer* 1989;64:1914-21.
- [13] Simpson JF, Gray R, Dressler LG, Cobau CD, Falkson CI, Gilchrist K.W., Pandya KJ, Page DL, Robert NJ. Prognostic value of histologic grade and proliferative activity in axillary node-positive breast cancer: results from the Eastern Cooperative Oncology Group Companion Study, EST 4189. *J Clin Oncol* 2000;18:2059-69.

AUTHORS

**First Author** – Dr Navneet kumar,MS ,V S Hospital  
,Ahmedabad, nvntkumar5@gmail.com

**Second Author** – Dr Sumedha Mukherjee, MD , Dr BC Roy  
Institute of Pediatric Sciences, Kolkata,  
sumedhamkhrj@gmail.Com

**Correspondence Author** – Dr Navneet kumar,,MS ,V S  
Hospital, Ahmedabad, nvntkumar5@gmail.com, (09825968906)