



Research Article

A STUDY ON TREND OF HORMONE RECEPTOR & HER-2/neu
EXPRESSION IN BREAST CANCER

P.Harisankar¹, G.M.Badhushah Mohideen Ibrahim²,
K.Karthikraja³, R.Baskaran⁴ and U.Manohar⁵

^{1,2,3,4} Department of General Surgery, Rajah Muthiah Medical College, Chidambaram.

⁵Department of Pathology, Rajah Muthiah Medical College, Chidambaram.

ARTICLE INFO

Article History:

Received 10th September, 2020

Received in revised form 22nd Sep., 2020

Accepted 15th October, 2020

Published online 28th October, 2020

Key words:

Breast Cancer, Hormone Receptors,
HER-2/neu Receptor

ABSTRACT

Background: Breast Cancer, the most common malignancy causing mortality in women, has its uniqueness in expressing Hormone Receptors - Estrogen and Progesterone Receptors & HER - 2/neu Receptor. These receptors play a key role in prognosis of the disease by affecting the disease progression and deciding the mode of treatment. The aim of this study was to analyze the prevalence of hormone receptor status & HER-2/neu Status in breast cancer. **Materials & Methods:** In the present study, immunohistochemical assay of 50 tumor block of patients of breast carcinoma was performed to know the ER, PR and HER-2/neu status as well as histological examination. **Results:** A total of 50 patients were included with a mean age of 48.9 years. The results in present study documented the 64%, 38% and 34% expression rate of Estrogen receptor (ER), Progesterone Receptor (PR) and Human epidermal growth factor receptor - 2 (HER- 2/ neu). An inverse correlation of ER with PR & HER-2/neu was observed. A significant association of Tumour size, lymph node involvement was observed with ER, PR & HER-2 / neu expression. **Conclusion:** In conclusion, the frequency of ER, PR & HER-2/neu Status in patients with breast cancer is almost same as reported in the literature. Hormone receptor and HER-2/neu receptor status are in inverse relationship. These findings have important implications for ensuring appropriate choices of treatment.

Copyright © 2020 Dr.P.Harisankar and Dr.G.M.Badhushah Mohideen Ibrahim et al this is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

INTRODUCTION

Breast carcinoma is the most common malignant tumor and the leading cause of deaths due to carcinoma in women. It is more common in developed countries.¹; most common histologic type being, infiltrating ductal carcinoma.² The mainstay of breast cancer treatment is surgery when the tumor is localized, followed by chemotherapy (when indicated), radiotherapy and for estrogen receptor (ER) and progesterone receptor (PR) positive tumors, adjuvant hormonal therapy.³ Determination of estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor-2 (HER2) status in patients with breast cancer is now considered a standard due to their predictive and prognostic implications.³When compared to the Western population, Indian women show higher incidence of hormone receptor (HR)-negative breast cancer.⁴ Moreover, the incidence of HR-positive tumor increases with age whereas triple-negative breast cancer and HER2-positive tumor decrease. Thus, younger women harbor relatively more aggressive and advanced cancers with poor prognosis than older women.⁵ Nowadays, more importance is given to biological molecular prognostic factors because a significant number of patients

with early-stage breast cancer harbor microscopic metastasis at the time of diagnosis.⁴ Hormone receptors (ER and PR) and human epidermal growth factor receptor-2 (HER-2) are the most relevant clinical biomarkers that are widely used in stratifying breast cancer cases management.⁵ ER, PR, and HER2/neu are prognostic as well as predictive factors.⁶ The aim of this study is to analyze the frequency of these biomolecular markers in histopathological examination so that it can contribute to traditional clinical predictive factors.

MATERIALS & METHODS

The present study was carried out in in-patients of General Surgical ward of Rajah Muthiah Medical College, Chidambaram, who were diagnosed to have Breast Cancer after triple assessment during 2018 - 2019. A total of 62 were diagnosed of which 50 were found eligible for the study. Various patients', tumour and treatment related parameters were recorded after obtaining consent from the patients. The biopsy was analysed immunohistochemically for ER, PR and HER-2/neu expression. All cases were immunohistochemically evaluated for ER, PR, and HER2/neu expression using standard immunoperoxidase method. The tests were

*Corresponding author: P.Harisankar

Department of General Surgery, Rajah Muthiah Medical College, Chidambaram.

interpreted with internal controls. Immunostaining was carried out on thin sections of formalin-fixed, paraffin-embedded tissue with fixation within 1 h in 10% neutral buffered formalin for at least 6 h and no longer than 72 h. ER and PR were scored as per Allred score which is a semi-quantitative system that takes into consideration the proportion of positive cells (Proportion score – 0 for none positive cell, 1 for 1%, 2 for 1%–10%, 3 for 10%–33%, 4 for 33%–66%, and 5 for 66%–100% positive cells) and staining intensity (intensity score – 0 for no stain, 1 for weak, 2 for intermediate, and 3 for strong staining). The two scores were then summed to produce total scores of 0 through 8. A score of 0–2 was regarded as negative, while 3–8 as positive.^{7,8} HER2/neu scoring of IHC slides was done as per the recommended American Society of Clinical Oncology/College of American Pathologists (ASCO/CAP) guidelines 2013. Score 0 and 1 were interpreted as negative, score 2 as equivocal, and score 3 as positive.⁹

RESULTS

Baseline patient and tumour characteristics are shown in Table 1. In this study group with 50 patients of Breast Cancer, mean age of the patients was 48.9 years. The youngest patient with breast carcinoma was 32 years of age; the oldest being 72 years of age. Most of the patients belong to age group between 50-59 years of age (38%), in postmenopausal status (60%). Most tumours are in size between 2-5 cm, belonging to Stage III, with Nottingham Prognostic Index Score ranging from 3.4-5.4, and majority of tumours found to have lymphnode involvement. Receptor expression pattern is shown in Table 2. The present study shown majority of cases as **ER positive (64%), PR Negative (62%) & HER-2/neu Negative (60%)**. Of total 24% cases are Triple Negative Breast Cancer. ER Expression shows a positive association with increasing age, postmenopausal status, Tumour size and lymph node involvement.

Table 1 Patient & Tumor Characteristics compared with ER, PR & HER – 2 /neu status.

Parameters	ER Status		PR Status		HER-2/neu status		
	Positive	Negative	Positive	Negative	Positive	Negative	Equivocal
Age							
<40	6	1	4	3	5	2	0
40-49	8	4	4	8	5	7	0
50-59	13	6	8	11	5	11	3
60-69	4	5	3	6	2	7	0
>70	1	2	0	3	0	3	0
Menopausal status							
Pre	15	5	8	12	11	9	-
Post	17	13	11	19	6	21	3
NPI Score							
<3.4	9	6	6	9	3	11	1
3.4- 5.4	18	9	10	17	10	16	1
>5.4	5	3	3	5	4	3	1
Tumor size							
< 2 cm	7	2	6	3	2	7	-
2 – 5 cm	13	7	6	14	10	8	2
>5cm	12	9	7	14	5	15	1
AJCC Stage							
Stage I	7	2	6	3	2	7	-
Stage II	9	7	3	13	7	7	2
Stage III	16	9	10	15	8	-	1
Stage IV	-	-	-	-	-	-	-
Lymphnode involvement							
Yes	24	6	13	17	14	13	3
No	8	12	6	14	3	17	-

Even though PR Expression shown similar trend, the significance is lesser than ER expression. HER-2/neu receptor shown positive association with lymph node involvement, showing negative/ no association with other parameters.

Table 2 Distribution of ER, PR & HER-2/neu Status

Status	Estrogen Receptor	Progesterone Receptor	HER-2/neu Receptor
Positive	32 (64%)	19 (38%)	17 (34%)
Negative	18 (36%)	31 (62%)	30 (60%)

DISCUSSION

The global incidence of breast cancer is on rise, with an extra surge over Asian countries, especially in premenopausal women¹¹. 0.5 – 2% rise in annual incidence across India, even more in younger females less than 45 years.¹² Most Indian studies have shown mean ages ranging 48- 53 years⁽¹⁰⁻¹⁴⁾. Our study as well, shows a mean age of 48.9 years, reinforcing the fact that Breast cancer occurs in earlier decades than in Western Population.¹⁵ Most Western studies shown a mean age of around 60 years.^{16,17}

In the present study, most of the tumours are ER Positive (64%), PR Negative (62%) and HER-2/neu negative (60%). Hormone Receptor positive tumours are 68%, either ER or PR or both positive. In a study among 2001 Indian patients, Ghosh *et al.* have reported hormone responsive tumours in 51.2% patients.¹⁰ Ahmed *et al.* demonstrated ER, PR, HER-2/neu expression in 137 Yemeni women as 43.8%, 27% and 30.6% respectively.¹⁸ In the present study, HER-2/neu expression was seen in 34% cases which is higher than 22% reported by Ghosh *et al.* in 2001 Indian patients¹⁰, 30.6% by Ahmed *et al.*¹⁸ and lower than 38.9% as demonstrated by Faheem *et al.* in 1226 Pakistani women.¹⁹

Only HER-2/neu expressing tumours accounts for 6% of all tumours in our study. TNBCs compromise 10%-20% of all breast cancers in Western literature and are most aggressive with poor prognosis.²⁰ Comparing to Western Literature, Indian data show higher rates of TNBCs and this was also observed in our study (24%). The diagnosis of TNBC in Asian Women also suggests that genetic susceptibility may play a role.²¹ In the current era of targeted therapy, IHC and molecular studies are required for assessing diagnostic, predictive & prognostic markers²² of breast cancer.

CONCLUSION

Most of the tumours are expressing hormone receptors, especially Estrogen receptors and HER-2/neu Negative. Hence, these tumours are hormone responsive. The percentage of Triple Negative phenotype is relatively high when compared to the western population. HER-2/neu over expressing tumours are also low, rendering low percentage of people eligible for targeted therapy. Thus, these biomolecular predictive factors plays a key role in prognosis of breast cancer by affecting the plan of management.

References

1. Stewart WB, Wild CP. Vol. 5. Lyon: World Health Organization; 2014. Breast Cancer. World Cancer Report 2014; p. 362.
2. Kumar V, Abbas AK, Aster JC. 9th ed. Vol. 2. Philadelphia, USA: Elsevier Saunders; 2014. Robbins and Cotran Pathologic Basis of Disease; pp. 1051–68.

3. Geneva: World Health Organization; 2008. Cancer Control: Knowledge Into Action: WHO Guide for Effective Programmes: Module 4: Diagnosis and Treatment.
4. Esteva FJ, Hortobagyi GN. Prognostic molecular markers in early breast cancer. *Breast Cancer Res.* 2004;6:109–18. [PMCID: PMC400674] [PubMed: 15084231]
5. Sengal AT, Haj-Mukhtar NS, Elhaj AM, Bedri S, Kantelhardt EJ, Mohamedani AA, *et al.* Immunohistochemistry defined subtypes of breast cancer in 678 Sudanese and Eritrean women; Hospitals based case series. *BMC Cancer.* 2017;17:804. [PMCID: PMC5710067] [PubMed: 29191181]
6. Mehta S, Shelling A, Muthukaruppan A, Lasham A, Blenkiron C, Laking J, *et al.* Predictive and prognostic molecular markers for cancer medicine. *Ther Adv Med Oncol.* 2010;2:125–48. [PMCID: PMC3126011] [PubMed: 21789130]
7. Allred DC, Harvey JM, Berardo M, Clark GM. Prognostic and predictive factors in breast cancer by immunohistochemical analysis. *Mod Pathol* 1998;11:155-68.
8. Allred DC, Bustamante MA, Daniel CO, Gaskill HV, Cruz AB Jr. Immunocytochemical analysis of estrogen receptors in human breast carcinomas. Evaluation of 130 cases and review of the literature regarding concordance with biochemical assay and clinical relevance. *Arch Surg* 1990;125:107-13.
9. Wolff AC, Hammond ME, Hicks DG, Dowsett M, McShane LM, Allison KH, *et al* Recommendations for human epidermal growth factor receptor 2 testing in breast cancer: American Society of Clinical Oncology/College of American Pathologists clinical practice guideline update. *Arch Pathol Lab Med* 2014;138:241-56.
10. Ghosh J, Gupta S, Desai S, Shet T, Radhakrishnan S, Suryavanshi P, *et al.* Estrogen, progesterone and HER2 receptor expression in breast tumors of patients, and their usage of HER2-targeted therapy, in a tertiary care centre in India. *Indian J Cancer* 2011;48:391-6.
11. Manjunath S, Prabhu JS, Kaluve R, Correa M, Sridhar TS. Estrogen receptor negative breast cancer in India: Do we really have higher burden of this subtype? *Indian J Surg Oncol* 2011;2:122-5.
12. Rajan G, Culas TB, Jayalakshmy PS. Estrogen and progesterone receptor status in breast cancer: A cross-sectional study of 450 women in Kerala, South India. *World J Surg Oncol* 2014;12:120.
13. Singh R, Gupta S, Pawar SB, Pawar RS, Gandham SV, Prabhudesai S. Receptor expression in patients in semi urban India. *J Cancer Res Ther* 2014;10:26-28.
14. Mukherjee G, Lakshmaiah KC, Vijayakumar M, Prabhu JS, Telikicherla D, Sridhar TS, *et al.* Analysis of clinico-pathological characteristics of Indian breast cancers shows conservation of specific features in the hormone receptor sub-types. *J Integr Oncol* 2016;5:159.
15. Bustreo S, Osella-Abate S, Cassoni P, Donadio M, Airolidi M, Pedani F, *et al.* Optimal ki67 cut-off for luminal breast cancer prognostic evaluation: A large case series study with a long-term follow-up. *Breast Cancer Res Treat* 2016;157:363-71.
16. Anderson WF, Pfeiffer RM, Dores GM, Sherman ME. Comparison of age distribution patterns for different histopathologic types of breast carcinoma. *Cancer Epidemiol Biomarkers Prev* 2006;15:1899-905.
17. Anderson WF, Reiner AS, Matsuno RK, Pfeiffer RM. Shifting breast cancer trends in the United States. *J Clin Oncol* 2007;25:3923-9.
18. Ahmed HG, Al-Adhraei MA, Al-Thobhani AK. Correlations of hormone receptors (ER and PR), Her2/neu and p53 expression in breast ductal carcinoma among Yemeni women. *Open Cancer Immunol J* 2011;4:1-9
19. Faheem M, Mahmood H, Khurram M, Qasim U, Irfan J. Estrogen receptor, progesterone receptor, and her 2 neu positivity and its association with tumour characteristics and menopausal status in a breast cancer cohort from northern Pakistan. *Ecancermedalscience* 2012;6:283
20. Gupta A, Jain J, Kumar A, Kumar S, Wadhwa N. Triple negative breast cancer – An overview and review of literature. *Asian J Med Sci* 2012;3:16-20.
21. Kakarala M, Rozek L, Cote M, Liyanage S, Brenner DE. Breast cancer histology and receptor status characterization in Asian Indian and Pakistani women in the U.S. – A SEER analysis. *BMC Cancer* 2010;10:191.
22. Krishnamurthy S, Poornima R, Challa VR, Goud YG. Triple negative breast cancer-our experience and review. *Indian J Surg Oncol* 2012;3:12-6.

How to cite this article:

Dr.P.Harisankar and Dr.G.M.Badhushah Mohideen Ibrahim *et al* (2020) ' A study on trend of hormone receptor & her-2/neu Expression in breast cancer ', *International Journal of Current Medical and Pharmaceutical Research*, 06(10), pp 5305-5307.
