A study on estrogen receptor, progesterone receptors, HER-2/NEU status in breast cancer cases attending to a tertiary care hospital of Andhra Pradesh

Prashanthi J[1], Ramaswamy Naik M[2]

[1]*Assisant Professor, Department of Radio therapy, [2]Professor and Head of Department of General Surgery, Government Medical College and General Hospital, Anantapuramu, Andhra Pradesh, India*

ABSTRACT

BACKGROUND: Breast cancer is one of the commonest form of cancer leading to considerable mortality and morbidity in developing countrylike India with age adjusted rate of 25.8 per 1,00,000 population.it is observed that expression of certain epidermal growth factor for certain receptors like Estrogen receptor(ER), Progesterone receptor(PR) and HER2/neu receptors are increased in certain malignancies, estimating which can help in preventive, promotive and therapeutic aspects of breast malignancy. **AIM:** the current retrospective study was undertaken to assess the ER, PR and HER – 2 / new states in breast carcinoma at Government Medical College and General hospital, Anantapuramu. An effort is made also to assess certain epidemiological factors associated with breast cancers.**RESULTS**: The current study indicated that mean age of presentation is 50. years. breast cancers are common in middle age group woman of rural areas who premenopausal and are have less than two children. The commonest histological type found is infiltrating ductal carcinoma(NOS) type. Hormone – expression in our study in low compared to western population but comparable with Indian studies.

Keywords: Breast cancer, Estrogen Receptor(ER), HER2/neu receptor, Progesterone receptor(PR)

Introduction

Carcinoma of breast per say, one of the commonest neoplasm presenting to any oncology/ department in the country. Breast cancer is adjudged as the commonest form of female cancer in India with a age adjusted rate as high as 25.8 per 1,00,000. The mortality resulting in Indian women because of Breast Cancer is estimated to about 12.7 per 1,00,000 women [1].

Breast cancer is supposed to be the commonest form of cancer among the women in the entire world and second commonest cancer after cervical cancer in Indian women. Breast cancer incidence is raising at an alarming rate in India and abroad in the last decade, increasing the burden of breast cancer deaths in lower socio-economic countries [2].

_____

*Correspondence
Dr. M. Ramaswamy Naik,
Professor and Head of General Surgery,
Government General Hospital, Anantapuramu, India
E-mail: dr.maheshgajula@yahoo.com

High levels of expression of either the epidermal growth factor receptor or the receptor-like HER2/*neu* gene product p185HER2 have been observed in a variety of human malignancies including breast cancer [3]. Hormone receptor status (Estrogen receptor & Progesterone receptor) & HER2 /neu expression form a very important prognostic markers in Breast cancer. Receptor positive cases have better prognosis compared to receptor negative cases [4] Triple negative Breast Cancer has worst prognosis [5]. Metastasis to lymph nodes in a breast cancer case forms one of the important prognostic factors [6]. Estrogen receptor(ER) & Progesterone Receptor(PR) status increased with advancing age [7]. Further it is postulated from the studies that breast feeding has protective effect against hormone receptor negative breast cancer [8-9]. With the aforementioned background, the current study is under taken to asses the hormone receptor status in breast cancer patients attending to Government Medical College and General Hospital.

Materials and methods

The Current a retrospective study was under taken after obtaining clearance from Institutional Ethics Committee at Cancer Unit, Department of Radiotherapy in association with Department of General Surgery, Government Medical College and General Hospital, Anantapuramu from February 2013 to February 2015. The study included a total number of ninety-seven subjects surviving with unilateral breast cancer of which all were females. Patients with incomplete information were excluded.

The data of patients is collected from patient records after obtaining consent with respect to patient age, tumor size, stage, estrogen and progesterone receptor status and HER 2/neu status was evaluated by immunohistochemistry. All the data is collected from the subjects in a pretested proforma and analyzed systematically by using appropriate statistical methods.

Observations and Discussion

Distributions of cases as per age of patients: It is evident from Table No.1 that most common age of presentation was in 45 to 55 decades of life and median age of presentation was 52.7 years (range 28 to 75 years). 64.6 % of patients were post-menopausal. similar findings are noticed in a study conducted by Porter etal [10] and Leong etal [11]. From the data it is evident that the incidence is quite common in the early middle age when compared to extremes of age. The median age of presentation in our study was 52 years and peak prevalence was found in the 45 to 55 years age group. Median age at diagnosis of cancer breast in the US was 61 yrs. Breast cancer occurs a decade earlier in Indian population [12].

Table No.1: Distribution of cases as per age		
Age group	**Total(n)**	**Percentage (%)**
25-35	7	7.21
36-45	22	22.68
46-55	32	32.98
56-65	22	22.68
66-75	13	13.40
75-85	01	1.03
Total	**97**	**100**
Mean	**50**	
Median	**52.7**	

Distribution of Subjects as to place of residence (Table -2): It is observed from the study that 49 subjects amounting to 51.44% are hailing from rural areas while 48.56%(48) subjects belong to urban areas. usually it is evident that the incidence used to be less is rural areas due to adherence to the rural life style **[13].** However, it is observed in the trends that the incidence is comparatively more in the rural areas and this observation may be attributed to the reasons such as low educational status, lack of awareness regarding the disease, lack of medical facilities for diagnosis and due to life style modifications. similar findings are noticed in the studies conducted by other authors [14-15].

Table:2 Distribution of study subjects according to Place of residence		
Place of residence	**No of study subjects**	**%**
Urban	48	48.56
Rural	49	51.44
Total	97	100

Breast Cancer and Socio-economic status (Table - 3): Findings of the current study indicates that the incidence of breast cancer is common in richer socio-economic sections of the society as observed in 65.44%(n=159) of cases in comparison to poorer section of society. This fact may be attributed to the dietary habits such as high fat diet, less house hold/physical activity and associated factors. similar findings are observed in a study conducted by [16]. Socio-economic status depicted in the table is based on the white card issued by Government of Andhra Pradesh to the below poverty line population.

Table:3 Distribution of study subjects according to Socio-economic status

Socio-economic status	No of study subjects(n)	Percentage(%)
Upper and middle class	63	65.44
Lower class	34	34.66
Total	97	100

Relation of breast cancer cases to menopause: It is evident from Table -4 that breast cancer is common in premenopausal women when compared to postmenopausal women amounting to 62.88% and 38.22% respectively. It can be stated that breast cancer is common in menstruating women and further it is observed that the women with two or less that two children are at increased risk when compared to women having 3 or more children. Similar findings are noticed in studies conducted elsewhere [17-18]. the exact reason for this is not known.

**Table:4 Distribution of study subjects according to status of Menopause**

Status of menopause	No of study subjects(n)	Percentage (%)
Pre-menopausal	61	62.88
Post-menopausal	36	38.22
Total	97	100

Distribution of cases asper histo-pathology of cancerous lesion: It can be inferred from Table-5 that Histopathology showed infiltrating ductal carcinoma (IDC not otherwise specified (NOS)) was the commonest variant comprising of 94.2 % of cases. Similar findings were noticed in study conducted by Victor J etal [19]. This finding will help to stratify the risk of cancers and aid to take preventive and promotive measures to reduce morbidity arising from breast cancers. Further it is observed in the study that most common pathological nodal stage was N_1 followed by N_0 (graph-1). These results are comparable to a study conducted by Bartelink H etal [20]. Most common pathological T stage was T_2 followed by T_3, T_4 and T_1 . 14(14.3%) cases showed distant metastasis.

Table:4 Distribution of study subjects according to histopathology

Histopathology	No of study subjects(n)	Percentage (%)
Infiltrating ductal carcinoma not otherwise specified(NOS))	91	94.22
Others	07	5.88
Total	97	100
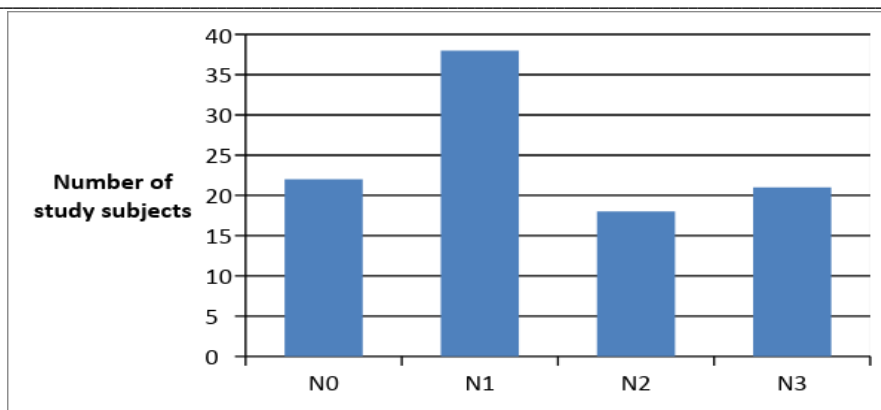
Graph-1 Nodal staging

Distribution of cases as per Receptor status: It can be deduced from table-5 that 50.51 % of cases are ER positive. 49.48 % of cases are ER negative. 48.45 % of case are PR positive. 51.54% cases are PR negative. 34.02 % of cases expressed HER -2 /neu receptor and 65.97 % are HER- 2 /neu negative. Of these 26.8 % cases are triple negative. Hormone receptor status is an important prognostic factor in breast cancer. Breast cancer patients that are ER and PR positive have lower rate of mortality compared to hormone receptor negative patients [21]. Our study showed that 50.5 % of cases had ER expression while 48.4 % expressed PR. This is lower compared to Western studies which have reported 73 % ER expression and 58 % PR expression [22]. but comparable to other Indian studies [23]. HER2 / neu positivity was present in 34.02 % of our cases. In western studies these values ranged from 17 % to 27 % [24]. HER2 / neu positive cases respond to Tramstuzumab. 26.8 % of cases are triple negative in our study. These case of have poor prognosis

Table-5: Distribution of Study Subjects as per Receptor status

Type of receptor	Positive		Negative	
	No. of subjects(n)	Percentage (%)	No. of Subjects(n)	Percentage (%)
Estrogen Receptor(ER)	49	50.51	48	49.48
Progesterone Receptor(PR)	47	48.45	50	51.54
HER2/neu receptor	33	34.02	64	65.97
Triple Negative	26(26.8%)			

Conclusion

Hormone receptor positive status in breast cancers is low as observed in our study when compared to western population but however the status is comparable to other studies done over Indian population. HER- 2/ neu expression is higher in our study compared to western studies and triple negative cases are also high compared to western population. Further we would like to conclude that breast cancers are common in middle age group woman of rural areas who premenopausal and are have less than two children. The commonest histological type found is infiltrating ductal carcinoma (NOS) type.

References

1. Gupta A, Shridhar K, Dhillon PK. A review of breast cancer awareness among women in India: Cancer literate or awareness deficit. European Journal of Cancer. 2015 Sep 30;51(14):2058-66.

2. Jemal A. Bray F, Center MM, Ferlay, J Ward E, Forman D et al. Global Cancer Statistics CA: A Cancer Journal for Clinicians 2011;61:69 – 90

3. Fendly BM, Winget M, Hudziak RM, Lipari MT, Napier MA, Ullrich A. Characterization of murine monoclonal antibodies reactive to either the human epidermal growth factor receptor or HER2/neu gene product. Cancer research. 1990 Mar 1;50(5):1550-8.

4. Ching – hung Lin, Huang – chun Lein, Fu-chang Hu, Yenshen Lu, Sung-hsin Kuo, Ling chu Wes et al, Fractionated evaluation of immunohistochemical hormone receptor expression enhances prognostic prediction in breast cancer patients treated with tamoxifen as adjavant therapy: J. Zhejiang Univ Sci B. 2010;11 (1): 1-9.

5. Gluz O, Liedtke C, Gottschalk N et al. Triple negative breast cancer. Current status and further directions, Ann Oncol 2009: 20 : 1913-1927

6. Jatoi I, Hilsenbeck SG, Clark GM, Os borne CK. Significance of axillary lymph node metastasis in primary Breast Cancer. J. Clin. Oncology 1999, 17 : 2334- 40

7. Hormone receptor status of breast cancer in India. a study of 98 tumors S.B Desai. RF Chinoy. The Breast. Volume 9 issue 5, October 2000, Pages 267 – 270.

8. Anderson KN, Schwab RB, Martinez ME. Reproductive risk factors & breast cancer subtypes a review of literature Breast Cancer Res Treat 2014; 144, 1-10.

9. F. Islami, Y Liu, A. Jernal et al - Breast feeding & Breast cancer Risk by receptor status – A systematic review and meta-analysis.

10. Porter PL. Global trends in breast cancer incidence and mortality. Salud P´ublica de México 2009; 51: s141–s46.

11. Leong SP, Shen ZZ, Liu TJ et al. Is breast cancer the same disease in Asian and Western countries? WorldJSurg2010; 34: 2308–24.

12. Lakhmini. K.B. Mudduwa. Quick score of hormone receptor status of breast carcinoma: Correlation with other clinicopathological prognostic parameters. Indian Journal of Pathology and Microbiology, 2009;52(2):p159-63.

13. Nagrani RT, Budukh A, Koyande S, Panse NS, Mhatre SS, Badwe R. Rural urban differences in breast cancer in India. Indian J Cancer 2014; 51: 277–81.

14. Ali I, Wani WA, Saleem K. Cancer scenario in India with future perspectives. Cancer Therapy 2011; 8: 56–70.

15. Srinath Reddy K, Shah B, Varghese C, Ramadoss A. Responding to the threat of chronic diseases in India. Lancet 2005; 366: 1744–9.

16. Paymaster JC, Gangadharan JC. Epidemiology of breast cancer in India. J Natl Cancer Instit 1972; 48: 1021–24.

17. Murthy NS, Agarwal UK, Chaudhry K, Saxena S. A study on time trends in incidence of breast cancer: Indian scenario. Eur J Cancer Care (Engl) 2007; 16: 185–6.

18. Surakasula A, Nagarjunapu GC, Raghavaiah KV. A comparative study of pre- and post-menopausal breast cancer: risk factors, presentation, characteristics and management. J Res Pharm Pract 2014; 3: 12–8.

19. Victor J, Aligbe JU. Histopathological types of breast cancer in Nigerian women: a 12-year review (1993-2004). African journal of reproductive health. 2006;10(1):71-5.

20. Bartelink H, Fentiman IS, Lerut T, Mignolet F, Olthuis G, Sylvester R, Winter J. Randomized clinical trial to assess the value of breast-conserving therapy in stage I and II breast cancer, EORTC 10801 trial. Journal of the National Cancer Institute. Monographs. 1992(11):15-8.

21. Lisa K. Dunn Wald, Mary Anne Rossing and Christopher I Li. Hormone receptor status, tumor characteristics and prognosis: a prospective cohort of breast cancer patients : Breast Cancer Res: 2007;9(1):R6

22. Rhodes A, Jasani B, Balaton AJ, Barnes DM, Miller KD. Frequency of oestrogen and progesterone receptor positivity by immunohistochemical analysis in 7016 breast carcinomas: Correlation with patient age , assay sensitivity, threshold value and mammographic screening. J. Clin Pathol 2000;53 :688-96

23. Ajith Vettuparambil, Ravindran Chirukandath, Terence B et al, Hormone receptor expression and survival patterns in operated cases of female invasive ductal breast carcinoma in Kerala – a retrospective cohort study – World J . Surg Oncology. 2015; 13:160.

24. Adedayo A. Onitilo, Jessica M. Engel , Robert T. Greenlee, Bickol N. Mukesh. Breast Cancer subtypes based on ER/PR and HER-2/neu expression. Comparison of clinicopathological features and survival. Clinical Medicine and Research 2009:7(1):7