International Journal Dental and Medical Sciences Research (IJDMSR)
ISSN: 2393-073X Volume 4, Issue 11 (November - 2020), PP 05-09
www.ijdmsr.com

The Natural History of Hormone Receptor- status Breast Cancer at a Tertiary Care Hospital of Kashmir India.

Dar Abdul Waheed[1], Mushood Ghulam Nabi[2], Lone Mustaq Ahmad[3], Kuchay Sonaullah[4], Lone Yasir Iqbal[5], Rahila Salaam[6].
Senior resident[1], Associate professor[2], professor[4], resident[6]
Department of radiation oncology GMC Srinagar Kashmir,
Associate professor[3] department of General medicine GMC Anantnag Kashmir,
Senior resident[5] Department of General Surgery GMC Srinagar Kashmir.
**Corresponding Author: Lone Mustaq Ahmad[3]*

ABSTRACT
Background:- Hormone receptor status and HER2 status are of critical interest in determining the prognosis of breast cancer patients. Their status is routinely assessed by immunohistochemistry (IHC). Classification of breast cancer into intrinsic subtypes has clinical and epidemiologic importance. To examine accuracy of IHC-based methods for identifying intrinsic subtypes, a three-biomarker IHC panel was compared with the clinical record.
Objective:- The aim of the present study was to analyze the Natural History of Hormone Receptor status breast cancers in Kashmir valley.
Materials and methods:
This was an observational chart based study conducted at government medical college Srinagar kashmir india from Jan 2015–dec 2018. One hundred fifty one biopsy proven cases of breast carcinoma were reviewed. Immunohistochemistry was used to evaluate the expression of Estrogen receptors(ER) and progesterone receptors (PR) and Her2Neu oncoprotein. Grade of tumour was assessed by Scarf Bloom Richerdson Grading system.
Results:- Total of 151 patients with histopathologically confirmed as Breast cancer cancers formed the study population. The female to male ratio in gastric cancers was 24.2:1. The age group varied from 16 to 80 years with most common age group in breast cancer was less than 45 years. The most common histopathological type of breast cancer detected was Invasive ductal carcinoma in 148(98%) patients followed by lobular carcinoma in 3(2%) patients. Considering ER, PR and Her2Neu oncoprotein overexpression and grade of tumour, overall majority of patients 42 (28%) presenting ER/PR positive followed by 41 cases (27%) had triple negative morphology.
Conclusion;- The College of American Pathologists and American Society of Clinical Oncology recommend ER and PR testing for all newly diagnosed cases of invasive breast cancer.IHC has become an integral part of the pathology laboratory. It is a more mature technology and accessible to the majority of pathology laboratories. IHC can be used for diagnostic issues, estimating prognosis or predicting response to therapy. Once these parameters are standardized, IHC will assume a better and well-defined role in the management of patients with cancer.

I. INTRODUCTION

Globally Breast Cancer is the leading cancer found among women. It is well known fact that cancer is an age-related disease which holds well even so in breast cancer.Breast cancer is the most frequently diagnosed cancer in women, and it is estimated that there will be 252,710 new cases of invasive breast cancer and 63,410 new cases of *in situ* breast cancers among women in the United States in 2017(**Siegel RL et al 2017)**[1] .In contrast to the significant number of breast cancer cases in women, it is expected that 2,470 cases of breast cancer will be diagnosed in men in 2017, with approximately 460 breast cancer deaths in men. There is considerable geographic, ethnic, and racial variability in breast cancer incidence. Ethnicity and national origin rank highly as predictors of risk for breast cancer, with up to a 10-fold variation throughout the world. **(MacMahon B et al 2006)**[2].

Prognosis and management of breast cancer is influenced by the classical variables such as histological type and grade, tumour size, lymph node status, and status of hormonal receptors, Estrogen receptors (ER) and progesterone receptors (PR) of the tumour and more recently Her2Neu oncoprotein status**.(Sharif MA et al 2009)**[3] . ER positive tumours (80% of breast cancer) use the steroid hormone estradiol as their main growth stimulus; ER is therefore direct target of endocrine therapies. PR expression is strongly dependent on the

presence of ER. Tumours expressing PR but not ER are uncommon and represent <1 % of all breast cancer**.(Weigol MT et al 2010)**[4]. The proto–oncogene(C–erb) has been localized to chromosome 17q and encodes a transmembrane tyrosine kinase growth factor receptor. Her–2 Neu amplification occurs in about one quarter to one fifth of breast cancers**.(Huang HJet al 2005)**[5] .Triple-negative breast cancer (TNBC) accounts for approximately 15% of breast cancers. TNBC is a poor prognostic factor for disease-free and overall survival, **(Kaplan HG et al 2006)**[6]. no effective specific targeted therapy is readily available for TNBC, **(Anders CK et al 2009)**[7] .Therefore this study intends to analyze the age at presentation, and hormone receptor status in patients with breast cancer which could help frame policies to help control and reduce the stage of this disease when diagnosed.

II. MATERIALS AND METHODS

This was an observational chart based study on breast cancer patients aged above 18 years of age who were diagnosed with either invasive or in situ breast cancer at government medical college Srinagar kashmir The duration of study was from June 2015 to December 2018. Clinically suspected breast carcinoma subsequently proved to be non-malignant lesions after histological examination; non-Hodgkin lymphoma and other non epithelial tumors of the Breast were excluded from this study. A retrospective study was conducted to find the Information regarding age, sex, clinical presentation histopathological type, and hormonal status of diseases. Scrutinization of all available records was done to get relevant information.

Statistical analysis

Descriptive analysis was used to report the study results. Categorical data were summarized as percentages. We analyzed the cancer characteristics according to age and sex. The aim of the present study was to analyze the receptor morphology of breast cancers in Kashmir valley.

III. RESULT:

Total of 151 patients with histopathologically confirmed as Breast cancer cancers formed the study population. The female to male ratio in gastric cancers was 24.2:1. The majority of the patients 46% in female were in < 45 years of age and in male were in >45 years in age; with males and females constituting 4% and 96% of patients in their respective groups. The age group varied from 16 to 80 years with most common age group in breast cancer was less than 45 years, followed by were in age 45-64years. Less than 45 years were in age group constituted 46% of the cases. Majority of patients had ECOG performance score I (50%) followed by 0 (30%). Married women were 148 (98.00%), and 3(2%) were unmarried. The salient observations of the study are shown in table 1.

Table 1: Demographic profile

Age	**N**	**%**
<45	69	46
45-64	61	40
>64	21	14
Gender		
Male	6	4
Female	145	96
Performance score		
0	45	30
I	75	50
II	21	14
III	10	06
Mariatal status		
married	148	98
Un married	3	2
total	151	100%

The most common histopathological type of breast cancer detected was Invasive ductal carcinoma in 148(98%) patients followed by lobular carcinoma in 3(2%) patients. Considering ER, PR and Her2Neu oncoprotein overexpression and grade of tumour, overall majority of patients 42 (28%) presenting ER/PR positive followed by 41 cases (27%) had triple negative morphology and 25 cases (16%) had her 2- neu

positive morphology, however 13 patients (9%) had ER positive and 10 patients (7%) had PR positive Receptor status morphology alone respectively, 20 patients (13%) had triple positive morphology shown in table 2.

Table 2:- Receptor status

RECEPTOR STATUS		
ER/PR POSTIVE	42	28
ER POSITIVE	13	9
PR POSITIVE	10	7
Her 2 NeU POSITIVE	25	16
TRIPLE POSITIVE	20	13
TRIPPLE NEGATIVE	41	27
TOTAL	151	100

Treatment modalities: - Treatment plan was made according to the stage of presentation assessed by clinical examination, radiological findings. Operability and type of surgery was assessed by the operating surgeon by clinical examination and examination under anesthesia. neoadjuvant, adjuvant chemotherapy/ hormonal treatment and radiotherapy was given according to protocols.

IV. DISCUSSION

Globally Breast Cancer is the leading cancer found among women. It is well known fact that cancer is an age-related disease which holds well even so in breast cancer. Breast cancer is the most frequently diagnosed cancer in women, and it is estimated that there will be 252,710 new cases of invasive breast cancer and 63,410 new cases of *in situ* breast cancers among women in the United States in 2017(**Siegel RL et al 2017)[1].**

The present study included 151 patients of breast cancer. A study by Hirko K *et al*[8]. noted that their study results showed a steep increase in breast cancer cases from 2009 to 2015 especially among women aged 30–39. Our study was similar to a study conducted by Hirko K *et al* that, the age group varied from 16 to 80 years with most common age group in breast cancer was less than 45 years, followed by were in age 45-64years. Breast cancer in men is rare, accounting for less than 1% of breast cancer cases in the US(Anderson WF et al)[9]. In contrast to the significant number of breast cancer cases in women, it is expected that 2,470 cases of breast cancer will be diagnosed in men in 2017, with approximately 460 breast cancer deaths in men. A study conducted by Anderson WF et al, since 1975, the incidence rate has increased slightly, from 1.0 case per 100,000 men during 1975-1979 to 1.3 cases per 100,000 men during 2010-2014. Our study was similar to Anderson et al, that the, males and females constituting 4% and 96% of patients in their respective groups.

Breast cancer is the most common cancer with increased mortality rate. In addition to pathological grade and stage, breast cancers are routinely assessed for hormone receptor status ER and PR by immunohistochemistry and human epidermal growth factor receptor2 (HER2) expression by IHC or amplification by FISH in order to guide the choice of the appropriate adjuvant therapy. A study conducted Davies C et-al[10], by Approximately 70% of human breast tumors express hormone receptors (HRs)—the estrogen receptor (ER) and/or the progesterone receptor (PR); these are the primary transcription factors driving oncogenesis in HRpositive (HR+) breast cancers. Both are targets of and predictors of response to anti-estrogen therapy. Present study was similar, According to receptor status in breast cancers, overall majority of patients 42 (28%) presenting ER/PR positive followed by 41 cases (27%) had triple negative and 25 cases (16%) had her 2- neu positive, however 13 patients (9%) had ER positive and 10 patients (7%) had only PR positive Receptor status.

Thirteen patients (9%) had only ER positive in our study, Which was contradicted to many international and local studies. The study conducted by Fatima et al.[11] also showed ER positivity to be 52.4%.Similarly a study conducted in India by Desai et al.[12] , showed ER positivity in 33% of cases, 46% were PR positive. In their study ER and PR immune reactivity increased with advancing age. Ranatunga et al[13] observed ER and PR positivity in 53% and 50% of cases respectfully. Yip et al.[14] reported that 50% of the cases were ER positive. Ong et al.[15] reported 60% of the cases were ER positive. This may be because of the reason that most of the patients in our study were between 25–45 years and in premenopausal age group where ER positivity is lower and it increases in post– menopausal age group and carcinomas were of high grade.

Considering the joint ER and PR positivity, overall majority of patients 42 (28%) presenting ER/PR positive in our study which was quite comparable to many international and local studies. while in the study by Desai et al.,[25] it was 25%. In study by Ranatunga et al.[13] it was 44%. While in local studies like Sharif et al.[16] the joint expression was 73.8% which is quite higher. A study conducted by Geethamala ET al[17], it was 52% while by Bhagat et al,[18] it was 36.2%.

The frequency of Her2/Neu reactivity is 25 cases (16%), which is very much lower to many international and local studies. In a study by Sharif et al.[16] the Her2/Neu positivity was seen in 31% of cases. In a study conducted by Geethamala et al[17] it was 25%.

In our study triple positive cases were 13%, while as in studies conducted by Geethamala Et al[17],triple positive had 5.5 % with grade 2 and 3.3% with grade 3 which was quite lower than in our study. In our study triple negative cases were almost 41 case (27%) and were of all grade 3, our study was contradicted to other studies like a study conducted by Suvarchala et al.[19] its quite higher, 42.1% as compared to other studies, conducted by **Bhagat et al.**[20] which revealed triple negative cases are 25.86%.

In our study most tumours were of grade 2 which is again in concordance with many of the studies like a study conducted by **Suvarchala et al**[19] tumour grades were of 43%, a study by Bhagat et al.[20] tumour grades were of (42%) **.**

V. LIMITATIONS

The limitations of our study are, more often the patients are referred to outside state , and most of patients were registered and treated at other cancer centre Skims kashmir valley. Hence, our study group may not exactly reflect (analyze) the Natural History of Hormone Receptor status breast cancers in Kashmir valley . Despite these limitations, our institution being a major oncological centre in this region, it may reflect the nature of the disease in this population and emphasizes the significance of early diagnosis by proper and timely evaluation, and management of the disease.

VI. CONCLUSION

The College of American Pathologists and American Society of Clinical Oncology recommend ER and PR testing for all newly diagnosed cases of invasive breast cancer.IHC has become an integral part of the pathology laboratory. It is a more mature technology and accessible to the majority of pathology laboratories. IHC can be used for diagnostic issues, estimating prognosis or predicting response to therapy. Once these parameters are standardized, IHC will assume a better and well-defined role in the management of patients with cancer. It is clear that the present study reveals majority of paients had ER/PR positive status followed by triple negative. With regard to subtypes, while the majority of scientists were against the requirement of multi-gene expression array profiling for subtype definition, approximately half the panel of St. Gallen 2013 opted for the use of a clinic-pathologic definition as sufficient for subtype definition. In conclusion, only ER, PR, Ki-67 and Her-2/neu are recommended for clinical use.

REFRENCES

[1]. Siegel RL 2017, Miller KD, Jemal A. Cancer Statistics, 2017. CA Cancer J Clin 2017;67(1):7–30.).
[2]. MacMahon B. Epidemiology and the causes of breast cancer. Int J Cancer 2006;118(10):2373–237)
[3]. Sharif MA, Mamoon N, Mushtaq S, et al. Morphological profile and association of Her–2 Neu with prognostic markers in breast carcinoma in Northern Pakistan. J Coll Phy Surg Pak. 2009;19(2):99–103.
[4]. Weigol MT, Dowsett M. Current and emerging biomarkers in breast cancer: prognosis and prediction. Endocr Relat cancer. 2010;17(4):245–262.
[5]. Huang HJ, Neven P, Drijkoningen M, et al. Hormone receptors donot predict the Her2/neu status in all age groups of women with an operable breast cancer. Ann Oncol. 2005;16(11):1755–1761.
[6]. Kaplan HG, Malmgren JA., Atwood MK. Impact of triple negative phenotype on breast cancer prognosis. Poster presented at: 29th Annual San Antonio Breast Cancer Symposium; December 14-17, 2006; San Antonio, TX.
[7]. Anders CK, Carey LA. Biology, metastatic patterns, and treatment of patients with triple-negative breast cancer. Clin Breast Cancer. 2009; 9(suppl 2): S73-S81.3.
[8]. (Hirko KA, Soliman AS, Hablas A, Seifeldin IA, Ramadan M, Banerjee M, Harford JB, Chamberlain RM, Merajver SD. Trends in breast cancer incidence rates by age and stage at diagnosis in gharbiah, Egypt, over 10 years (1999–2008). Journal of cancer epidemiology. 2013.
[9]. Anderson WF, Jatoi I, Tse J, Rosenberg PS. Male breast cancer: a population-based comparison with female breast cancer. J Clin Oncol. 2010;28: 232-239.
[10]. Davies C, Godwin J, Gray R, et al. Relevance of breast cancer hormone receptors and other factors to the efficacy of adjuvant tamoxifen: patient-level metaanalysis of randomised trials. Lancet. 2011;378:771-84
[11]. Fatima S, Faridi N, Gill S. Breast cancer. Steroid receptors and other prognostic indicators. J Coll Phy Surg Pak. 2004;15(4):230–233 .
[12]. Desai SB, Moonim MT, Gill AK, et al. Hormone receptor status of braest cancer in India: A study of 798 tumours. Breast. 2000;9(5):267–270.

[13]. Ranatunga N, Liyanapathirana LV. Hormone receptor expression and Her2 /neu amplification in breast carcinoma in a cohort of Srilankans. Ceylon Med J. 2007;52(4):133–136.
[14]. Yip CH, Taib NA, Mohamed I. Epidemiology of breast cancer in Malaysia. Asian Pac J Cancer Prev. 2006;7(3):130–133.
[15]. Ong TA, Yip CH. Short term survival in breast cancer: The experience of the university of Malaya Medical centre. Asian J Surg. 2003;26(3):169– 175
[16]. Sharif MA, Mamoon N, Mushtaq S, et al. Morphological profile and association of Her–2 Neu with prognostic markers in breast carcinoma in Northern Pakistan. J Coll Phy Surg Pak. 2009;19(2):99–103
[17]. Geethamala K, Srinivasa Murthy V, BR Vani, et al. Histopathological Grade versus hormone receptor status in breast carcinoma treasure the past. International journal of biomedical research. 2015;6(7):466–471.
[18]. Bhagat Vasudha M, Jha Bharti M, Patel Prashant R. Correlation of hormonal receptor and her2 neu expression in breast cancer: A study at tertiary care hospital in south Gujarat. National Journal of medical research. 2012;2(3):295–298
[19]. Suvarchala SB, Nageswararao R. Carcinoma breast–histopathological and hormone receptors correlation. J Biosci Tech. 2011;2:340–348.
[20]. Bhagat Vasudha M, Jha Bharti M, Patel Prashant R. Correlation of hormonal receptor and her2 neu expression in breast cancer: A study at tertiary care hospital in south Gujarat. National Journal of medical research. 2012;2(3):295–298.

Corresponding Author: Lone Mustaq Ahmad[3]
Associate Professor[3] Department Of General Medicine GMC Anantnag Kashmir,