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Original Research Article

A Study on the Correlation of Bloom-Richardson Scoring and Immuno-Histochemical Profiling in Breast Cancer at Government Medical College, Kota

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Abstract

Breast cancer occurs in every country in the word. Prognosis and management of breast cancer are influenced by classic variables such as grade, stage, hormone receptor status of estrogen, progesterone and Her2neu over expression. A study was conducted at M.B.S. Hospital and NMCH Hospital associated with Government Medical College Kota from 2018 to Sept 2019 in the department of Pathology with basic aim to ascertain correlation of various Histo-pathological score with ER, PR and Her2/neu receptor status of breast carcinomas. Maximum numbers of breast cancer patients were seen in 5th decade. ER and PR positivity was seen in 37.64% and 35.29% of cases. The hormonal expression in our study suggests that percentage of hormonal expression in India is lower when compared to western countries. ER and PR positivity was more commonly associated with small tumor size and low tumor grade and score signifying higher percentage of ER/PR positivity in differentiated tumors. HER-2/neu over expression was seen in 23.52% cases, these observations were similar to other international studies. HER-2/neu over expression was significantly associated with large tumor size and negative ER, PR status.

Keywords: Breast Carcinoma, Bloom-Richardson Grading, Immunohistochemistry (IHC), Estrogen Receptor (ER), HER2/neu Expression.

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Introduction

Breast carcinoma is the most common malignant tumor among women. It contributes to a significant proportion of all cancers in women worldwide (25%). Annually about one million women are diagnosed with breast cancer worldwide [1].

The incidence of breast cancer is greater in women of higher socio-economic background. High-risk areas include Europe and North America and the lowest rates are reported from Africa and Asia but nowadays the incidence of breast carcinoma has increased in less developed countries owing to gradual changes in lifestyle of women.

Many studies have been concerned about its pathogenesis, and biological behavior. It has been documented that breast cancer is a heterogeneous disease with variable biological and clinical characteristics because of its different genetic makeup [2,3], so it is difficult to predict the occurrence of distant metastases. Thus, there is a need for new and effective breast cancer therapies with existing ones. A crucial development in the evaluation of breast cancers has been the realization that the presence of hormone (estrogen and progesterone) receptors in tumour tissue correlates well with response to hormone therapy and chemotherapy [4,5].

Prognosis and management of breast cancer are influenced by classic variables such as grade, stage, hormone receptor status of estrogen, progesterone and Her2neu overexpression [6,7,8,9,10]. Prognostic factors are those which influences patient's overall outcome such as chances of recurrence after treatment.

These factors help in the selection of patients for a specific treatment [11]. Predictive factors evaluate the likelihood of benefit from a specific treatment. Estrogen receptors, Progesterone receptors, and HER2/neu are prognostic as well as predictive factors [12]. The basic aim of this study is to ascertain correlation of various Histo-pathological score with ER, PR and Her2/neu receptor status of breast carcinomas.

Material & Methods

Specimens of all patients of all age groups with breast cancer diagnosed and treated as lumpectomy and modified radical mastectomy at M.B.S. Hospital and NMCH Hospital associated with Government Medical College Kota, were included in this study. A combined prospective and retrospective study was conducted from Jan. 2018 to Sept 2019 in the department of Pathology. Modified radical mastectomy and lumpectomy specimen were subjected to routine histological examination and Immuno-histochemical analysis. Surgical specimens received in Department were subjected for routine histological examination and Immunohistochemical analysis. Clinical details were archived from the files. Specimen diagnosed as in situ malignancies / other atypical lesions, hyperplastic conditions of breast and stromal and metastatic malignancies of breast were excluded.

Results

Table 1: Distribution of patients according to age

Age in years	No of patients	Percentage
30-40	21	24.70%
41-50	34	40%
51-60	18	21.17%
61-70	10	11.76%
71-80	2	2.35%
Total	85	100%

The maximum no of cases were noted between 41 to 50 year of age (40%) followed by 30 to 40 years of age about 25%.

Table 2: Hormone receptor status of tumors in our study

Hormone receptor		Cases	Percent
ER	Positive	32	37.64%
	Negative	53	62.35%
PR	Positive	30	35.29%
	Negative	55	64.70%
ER/PR	ER+/PR+	30	35.29%
	ER+/PR-	2	2.35%
	ER-/PR+	0	0%
	ER-/PR-	53	62.35%

ER and PR expression was positive in 32 (37.64%) and 30 (35.29%) cases respectively. Simultaneous positive expression of ER, PR was found in 30 cases (35.29%) and 53 cases (62.35%) out of 85 cases were ER and PR negative.

Table 3: HER-2/neu receptor status of tumor cells in our study

HER-2/neu	Cases	Percent
Negative	58	68.23%
Positive	20	23.52%
Borderline	7	8.23%
Total	85	100%

Majority of the cases were Her2 neu negative in 68.23%. In about 8% cases the response of Her2 neu receptor was borderline.

Table 4: Intensity of HER-2/neu over expression in the breast cancer

The intensity of HER-2/neu over expression	Cases	Percent
0	52	61.17
1+	6	7.05
2+	7	8.23
3+	20	23.52
Total	85	100

HER-2/neu was positive (3+) in 20 (23.52%), equivocal (2+) in 7 (8.23%) and negative with score 0 (52 cases) and 1+ (6 cases) were reported in 61.17% and 7.05% cases respectively.

Table 5: Distribution of cases according to tumor size

Tumor size	No of cases	Percentage
T1 (<2cm)	9	10.58%
T2 (2-5 cm)	48	56.47%
T3 (>5 cm)	28	32.94%
Total	85	100%

Tumor size ranged from 1.5 to 12 cm. Out of 85 breast cancer 9 cases (10.58%) were of T1 category, 48 cases were (56.47%) under T2 and 28 cases (32.94) were in T3 category. More than half (56.47%) of tumors measured in T2 range (2cm-5 cm).

Table 6: Distribution of cases according to Nottingham Modification of Bloom Richardson (RB) scoring System

RB score		Cases	Percent
Tubule formation	1 point	3	3.52
	2 points	47	55.29
	3 points	35	41.17
Nuclear pleomorphism	1 point	17	20
	2 points	66	77.64
	3 points	2	2.35
Miototic count	1 point	44	51.76
	2 points	27	31.76
	3 points	14	16.47

A marked nuclear pleomorphism was seen in 2.35% of cases examined. Nuclear pleomorphism was either moderate or mild in the remaining cases (77.64% and 20% respectively).

Table 7: Correlation of Hormone receptor status [Estrogen and Progesterone Receptor Expression] with Tumor Grade and score (P value <0.05)

Tumor Grade		ER status		PR status	
		Positive	Negative	Positive	Negative
Grade I (3-5)	34 (40%)	17(50%)	17(50%)	16(47.05%)	18(52.94%)
Grade II (6-7)	41(48.23%)	14(34.14%)	27(65.83%)	13(31.70%)	28(68.29%)
Grade III(8-9)	10(11.76%)	1(10%)	9(90%)	1(10%)	9(90%)
Total	85	32	53	30	55

In grade I breast carcinoma (34 cases), ER positivity was observed in 17 cases (50.0%), PR positivity was observed in 47.05%. In grade II breast carcinoma (41 cases), ER positivity was observed in 14 cases (34.14%), PR positivity was observed in 13 cases (31.70%). In grade III breast carcinoma (10 cases), ER and PR positivity was observed in 1 case (10%). ER and PR expression were seen more frequently in grade I (score 3-5) tumors, compared to grade III (score 8-9) tumors.

Table 8: HER-2/neu over expression in relation to tumor grade and score (P value <0.05)

Tumor grade and score	HER-2/neu overexpression			Total Cases
	Positive	Negative	Borderline	
I (3-5)	6(17.64%)	25(73.52%)	3(8.82%)	34(40%)
II (6-7)	12(29.26%)	26(63.41%)	3(7.31%)	41(48.23%)
III (8-9)	2(20%)	7(70%)	1(10%)	10(11.76%)
Total	20(23.52%)	58(68.23%)	7(8.23%)	85(100%)

Her2neu positivity was increases from grade I (score 3-5) (17.64%) to grade III (score 8-9) (23.52%).

Table 9: Correlation between ER, PR & Her2 neu and BR grading and score

BR grade	ER		PR		Her2 neu			Triple +	Triple -	Cases
	+	-	+	-	+	-	Bor			
I (3-5)	17	17	16	18	6	25	3	1	11	34
II(6-7)	14	27	13	28	12	26	3	3	15	41
III(8-9)	1	9	1	9	2	7	1	0	6	10

Discussion

In this study there is correlated between BR scoring and Immuno-histochemical profiles of cases of breast cancer. Out of 85 cases, the age of patients ranged from 32 to 72 years. Age distribution

pattern of our study closely matches with studies conducted by Nikhra et al. [13] with range between 31 to 75years, and Mukherjee et al. [14] with range between 30-70 years. About 68% cases were below 50 years of age. These results was comparable with studies conducted by Nikhra et al. [13] with cases below 50 years of age were, 60.46% and Mukherjee et al. [14] 69.49% cases were below the age of 50 years. The mean age at presentation of breast cancer in our study was 48.92 years. Our finding are consist with Kamath et al. [15], Azizun-Nisa et al. [9], Nikhra et al. [13], and Munjal et al. [16] This may be attributed to hormonal changes that take place at particular age group of women which may act as nidus for breast cancer development.17The average age of occurrence of breast cancer amongst western females is 61.0 years.18The average age of occurrence of the breast cancer in India revealed that the disease occurs a decade earlier, as compared to western countries. [19,20]

In our study out of 85 cases, ER positive cases were 32 (37.64%) while PR positive cases were 30 (35.29%), triple positive cases were 4 (4.70%), triple negative cases were 32 (37.64%) and HER-2/neu over expression was seen in 20 cases (23.52%). Similar findings were also observed by Nikhra et al. [13] ER positivity was, 39.5%, PR positivity -41.86%, and HER-2/neu positivity - 32.55%. Only 9.3% cases were triple positive, and 32.5% cases were negative. Munjal et al. [16] observed that ER and PR positivity were 41.1%, and Her2neu+was 40.2%. Azizun- Nisa et al. [9] ER and PR were positive in 32.7% and 25.3% cases respectively. HER-2/neu was positive (3+) in 24.7%. Studied conducted in west contries showed that hormone receptor expression in India is lower as compared to the West, Shet et al. [21] (ER & PR +ve in 53.9%) and Priti Lal et al., [22] (73.65% ER positivity and 48.59% PR positivity).

In this present study, HER-2/neu over expression was seen in 23.5% cases. In the Western studies conducted by Taucher et al. [23], and Huang et al. [24] values ranged from 17 % - 27%. Study conducted by Ayadi L et al. [25] in Tunisia an Asian country and reported that HER-2/neu over-expression was 18.1%.

Tumor size is also one of the most important predictors of tumor behavior. In this study the tumor size more than 2 cm was seen in 89.41% cases. Our findings were similar to study of Azizun- Nisa et al. [9], found 88% cases of tumor size more than 2 cm, and Mala Mukherjee et al. [14], 94.92% were present with tumor size more than 2 cm. These results demonstrate that Indian women present at late stages of disease and hence have larger sized tumors. It was observed that most of the breast cancer cases present late to the hospital for diagnosis and treatment (NCRP, 2007) [26]. This happens because of lack of awareness, illiteracy, poor knowledge, not practicing self-breast examination and absence of national breast screening programmes in India. This reflects a need for promoting awareness programmes among women and to initiate national policies of screening for breast cancer. The studies from a western country show dissimilar results with tumor size smaller predominately less than 2 cm at the time of diagnosis or reporting to a medical facility. The study conducted by Taucher et al. [23], the tumor size was predominantly less than 2 cm in 59.9% cases. Gill et al [27]. Studied on Australia and France population with results, the size of tumor was, less than 2 cm in most of patients in breast cancer. This could be due to the widespread availability of mammographic screening programs and increased awareness in the Western countries.

In our study the grade I lesions was 34 cases, out of which ER and PR positivity was 50% and 47.05% respectively. The cases with grade II lesions were 41, ER and PR positivity was 34.14% and 31.70%. Out of 10 cases of grade III lesions the ER and PR positivity was 10 %. The study conducted by Mukherjee et al. [14] grade I lesions, ER and PR positivity was 85.7% and 78.5%. , grade II lesions ER and PR positivity was 75% and 71.88%, and grade III lesions, ER and PR positivity was 23.08 %. These results showed that hormonal receptor expression was inversely related to grading of the tumor.

This study contains Her2neu positivity increased from grade I (17.64%) to grade III (20%). These results consist with the study conducted by Mukherjee et al. [14]. Her2neu positivity increased from grade I (33.33%) to grade III (54.55%). Slamon et al [28] firstly observed that there is association between Her-2/neu gene amplification and poor prognosis of breast cancer.

Conclusion

Breast cancer is a heterogeneous disease with varied biological behavior and prognosis. The Bloom-Richardson grading remains an important histo-pathological method for assessing tumor differentiation, with advanced in molecular pathology, immuno-histochemistry has become essential for evaluating receptor status and guiding therapy in breast cancer. A significant correlation exists between Bloom-Richardson histological grading and immune-histochemical biomarker expression in the breast cancer. Integration of histopathological grading with immunohistochemical profiling provides valuable prognostic information and aids in individualized treatment planning.

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