Original Research Paper

Pathology

STUDY OF IHC MARKERS ER, PR, HER 2 NEU IN BREAST CANCER AND ITS RELATION TO TUMOR TYPE AND GRADE

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ABSTRACT **Background-** Thus the present study was done to study the IHC markers i.e ER, PR, HER2 NEU in breast cancer and its relation with type and grade of tumors **Methods-** The present study was conducted in the Department of Pathology, Jhalawar Medical College, Jhalawar, Rajasthan, India, to study the IHC markers i.e ER, PR, HER2 NEU in breast cancer and its relation with type and grade of tumors. The present study was conducted from January 2020 to October 2021. The total cases were 47 of any age group reporting to Department of Pathology were enrolled for the study. The study was carried out after obtaining approval from the Institutional Research Ethical Committee. An informed and written consent was obtained from all the patients. **Results-** Out of total 47 cases 65.95% cases were of ER negative, 34.04 % cases are of ER positive , 68.08% cases PR negative and 31.91% cases were PR positive. 80.85% cases were HER 2 neu negative and 19.14 cases her 2 neu positive. **Conclusion-** This study revealed that maximum cases were of modified radical mastectomy specimen of left side in which most of the cases were of Inavsiveduct carcinoma, moderately differentiated with MRB scoring of 6/9 and basal type of molecular type showing necrosis with maximum cases not showing skin and nipple invasion. We conclude that IHC classification as a clinical tool as ER/PR and Her 2 testing is widely available at a reasonable cost, is clinically used, therapeutically informative classification of breast cancer based on immunophenotype and is prognostic as well as somewhat predictive.

KEYWORDS : ER/PR, IHC, MRB

INTRODUCTION

Breast cancer is always develops silently. Mostly woman observe this pathology during their routine examination. Few may came to know about this when breast lump is accidentally discovered, or there is any change in shape or size of breast, or discharge in nipple. The condition of mastalgia is also commonly seen.[1]

In breast cancer a positive status of estrogen receptor is found to be linked with a good reply to therapy with hormones and linked to a better prognosis, a long disease-free survival. The added predictive and prognostic significance of the progesterone receptor is still a matter of controversy.[2]

A member of the Erb family called HER2 has a significant function to promote the transformation of oncogenic cells leading to tumor growth.3 In around 25% to 30% patients suffering with breast cancer the breast tumor over express HER2 protein, and this kind of overexpression is generally related to a decreased clinical outcome.4 This IHC-based classification is holding a significant importance in clinical practice, particularly when there is nonavailability of fresh tissue, and it is very well shown to be correlated with intrinsic classification by using microarrays of gene expression: ER/PR+, Her2− with Luminal A; ER/PR+, Her2+ with Luminal B; ER/PR−, Her2+ (ER−/Her2+) and ER/PR−, Her2− with triple negative/basal-like tumors.[5]

A considerable amount of interlaboratory and intralaboratory disparity was found in ER, that is caused due to antigen retrieval, fixation, and staining methods, that vary among different laboratories.6 Considerable discordance between the results of Her2 came from different laboratories taken from the same specimen has also been noticed. Because of that this classification seems to be more useful. Further efforts are need to be initiated for consistency of the recent testing techniques and improvement of more consistent and reproducible testing methods for ER/PR and Her2/ neu expression.[7]

MATERIAL AND METHODS

The study was carried out in Department of Pathology, Jhalawar Medical College, Jhalawar, Rajasthan, India to study of IHC markers ER, PR, HER 2 NEU in breast cancer and its relation to tumor type and grade . All participants submitted informed consent before enrolment.

Study Type- A hospital based cross-sectional study.
Place Department of Pathology, Jhalawar medical college, Jhalawar. Duration January 2020 to October 2021 year (duration includes time required for data collection, analysis and report writing).

SUBJECTS

All female patients of all age groups diagnosed with breast malignancy to the department of pathology, JMC, Jhalawar during this period.

INCLUSION CRITERIA:
Mastectomy specimen.
Modified radical mastectomy specimen.
Lumpectomy specimen.
True cut biopsy
Core biopsy

EXCLUSION CRITERIA:
Male breast specimen.

In situ carcinoma diagnosed cases.
Benign breast disease.
Inflammatory breast disease.
Inadequate specimen.

METHODOLOGY:-

After obtaining approval and clearance from the ethical committee, only those cases meeting the inclusion criteria was enrolled for the study.

After enrolment the following parameters were considered and/or measured in all patients: name, age, gender, religion, occupation, address, general physical examination. In this study, a total of 47 patients diagnosed with breast malignancy were assessed in the study at our Institute

RESULTS

Table no. 1 Distribution of study according to histologic subtype

Histologic subtype	Total no of cases	Percentage
Invasive duct carcinoma	34	72.34%
Invasive lobular carcinoma	09	19.14%
Solid papillary carcinoma	02	4.25%
Metaplastic carcinoma	01	2.12%
Invasive duct carcinoma with neuroendocrine differentiation	01	2.12%
Total	47	100%

Out of 47 cases maximum cases were of Invasive duct carcinoma 72.34%. 19.14% cases were Invasive lobular carcinoma 4.25% were solid papillary carcinoma. Metaplastic carcinoma (2.12%) Invasive duct carcinoma with neuroendocrine differentiation (2.12%).

Table no.2 Distribution of study according to grade of tumor

Grade of tumor	No of cases	Percentage
Well differentiated	10	21.2 %
Moderately differentiated	24	51.06%
Poorly differentiated	13	27.65%
Total	47	100%

Out of total 47 cases 51.06% cases were of moderately differentiated grade ,27.65% cases were of poorly differentiated, 21.2% cases were of well differentiated grade.

Table no. 3 Distribution of study according to MRB scoring

MRB Scoring	No of cases	Percentage
4/9	02	4.25%
5/9	08	17.02%
6/9	12	25.53%
7/9	11	23.40%
8/9	08	17.02%
9/9	06	12.76%
Total	47	100%

Out of total 47 cases 25.53% cases were of 6/9 ,23.40% cases of 7/9 scoring, 17.02% cases of 8/9,12.67% cases were of 9/9 ,17.02% cases of 5/9 ,4.25% cases of 4/9.

Table no. 4 Distribution of study according to ER, PR AND HER 2 neu marker

	ER	%	PR	%	HER 2 neu	%
Positive	16	34.04	15	31.91	9	19.14
Negative	31	65.95	32	68.08	38	80.85
Total	47	100	47	100	47	100

Out of total 47 cases 65.95% cases were of ER negative, 34.04 % cases are of ER positive ,68.08% cases PR negative and 31.91% cases were PR positive. 80.85% cases were HER 2 neu negative and 19.14 cases her 2 neu positive.

Table no.5 Distribution of study according to molecular subtype

Type of tumor	No of cases	Percentage
Luminal type A	13	27.65%
Luminal type B	03	6.38%
Her 2 neu enriched	09	19.14%
Basal type	22	46.80%
Total	47	100%

Molecular subtype 46.80% maximum cases were of basal type,27.65% cases of luminal type A ,19.14% cases of her 2 neu enriched and 6.38% cases were luminal type B.

DISCUSSION

Breast cancer is no longer seen as a single disease but rather a multifaceted disease comprised of distinct biological subtypes with diverse natural history, presenting a varied spectrum of clinical, pathologic and molecular features with different prognostic and therapeutic implications. Consensus regarding the definitive prognostic/predictive analysis has yet to be reached, but significant progress continues to be made in the ongoing search for a specific, rigorous and reproducible method of identifying successful treatment algorithms utilizing biological markers.[8]

A small number of single biomarkers, including estrogen receptor (ER), progesterone receptor (PR), human epidermal growth factor receptor-2 (HER2), and proliferation marker Ki-67 have been used for several years to predict the prognosis of breast cancer and to guide its therapy. The biological importance of these established markers has been reinforced over the past decade by the results from genomic classification.[9]

In present study, according to molecular subtype 46.80% maximum cases were of basal type, 27.65% cases of luminal type A, 19.14% cases of HER 2 neu enriched and 6.38% cases were luminal type B. In present study, according to MRB scoring, out of total 47 cases 23.40% cases were of 6/9, 23.40% cases of 7/9 scoring, 17.02% cases of 8/9, 12.67% cases were of 9/9, 14.89% cases of 5/9, and 4.25% cases of 4/9. We also assessed the molecular subtype according to grade of tumour.

Out of total 47 cases 65.95% cases were of ER negative, 34.04 % cases are of ER positive,68.08% cases PR negative and 31.91% cases were PR positive. 80.85% cases were HER 2 neu negative and 19.14 cases her 2 neu positive.Out of 47 cases, 5 cases were well differentiated in which 8.33% cases were luminal type A ,33.3% cases are luminal B 9.1% cases are basal type and 11.1% cases are of her 2 enriched. 23 were moderately differentiated in which 14.52% cases were luminal type A , 33.3% cases are luminal B,14.6% cases are basal type and 88.9% cases are of her 2 enriched. 14 cases were poorly differentiated in which maximum cases, 54.4 % were of basal type.

Similar results were observed in a study by **Al-Thoubaity FK et al.[9]** who found that Luminal A (58.5%) subtype was the most prevalent, followed by triple negative (16%), luminal B (14%), and HER2-positive (11.5%). **Jonnada PK et al.[10]** found that among molecular subtypes of breast cancer, luminal A was the most prevalent subtype followed by TNBC, luminal B, and HER2-enriched subtypes. The overall prevalence of TNBC in India is high compared to other regions of the world. Additional research is warranted to identify the determinants of high TNBC in India. Differentiating TNBC from other

molecular subtypes is important to guide therapeutic management of breast cancer.[88]

CONCLUSION

This study revealed that maximum cases were of modified radical mastectomy specimen of left side in which most of the cases were of Inavsiveduct carcinoma, moderately differentiated with MRB scoring of 6/9 and basal type of molecular type showing necrosis with maximum cases not showing skin and nipple invasion. We conclude that IHC classification as a clinical tool as ER/PR and Her 2 testing is widely available at a reasonable cost, is clinically used, therapeutically informative classification of breast cancer based on immunophenotype and is prognostic as well as somewhat predictive.

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