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Original Research Article

Correlation of ER & PR with proto-oncogene & grades of invasive duct carcinoma

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ABSTRACT

Background & Methods: The present study entitled "Correlation of ER & PR with proto-oncogene & grades of invasive duct carcinoma" was conducted in Dept. of Pathology, at SRMSIMS, Bareilly.
Result: The quick scoring of ER & PR is combination of proportion and intensity scoring. Out of 56 cases, 24 cases (42.85%) were ER negative & 22 cases (39.28%) were PR negative while both were negative in 18 cases (32.14%). There was a significant relationship between tumour grading & receptor status. As the grade of tumour increases ER & PR positivity decreases. Most of the tumour of grade 01 were both ER & PR positive. Here the value of ($p<0.05$) for both ER & PR which is significant.
Study Designed: Observational Study
Conclusion: For all invasive carcinomas, hormone receptor status is also studied using immunoperoxidase method and Quick scoring was done. Hormone receptor status was also correlated with other tumor characteristics as histological grading. Both ER & PR positive immune staining was observed in 71.42% cases of grade I, 64.10%casesof grade II were positive for ER & 25% were positive for PR and20% cases of grade III were found positive for ER & 10% was found positive for PR.

1. Introduction

ER-α is as a nuclear transcription factor activated by estrogen to regulate growth & differentiation of normal breast epithelial cells.[1] These pathways remain operative to varying degree of IBCs. ER-α expression has been measured in IBC's for almost 40 yrs. During first 20-25 years it was measured by radio labeled biochemical ligand (i.e. estrogen) binding assays (LBA's).

The primary reason for assessing ER-α is its ability to predict response to hormonal therapy like Tamoxifen.[2,3]

In 1990, research facilities around the globe deserted LBA for IHC as its capacity to quantify ER-α on routine formalin fixed paraffin inserted tests, killing the requirement for new solidified example and the framework needed to give it. Other bit of leeway of IHC incorporate lower cost, better well being just as unrivaled affect ability and that the appraisal of ER-α is confined to tumor cells under direct minute representation autonomous of tumor cellularity or the presence of generous epithelium, which is hazardous for LBA's.

IBCs express ER-α that is primarily atomic in location & that there is enormous variety between ER-α communicating tumor on a continuum going from 0 to almost 100% positive cells5. All the more ever they show an immediate connection between's the probability of clinical reaction to hormonal treatments and level of ER-α expression.[4]

The tumor communicating even exceptionally low levels (between 1 to 10% positive cells) show a huge advantage, far over that of ER-α negative tumors which are basically lethargic.

Evaluating ER-α by IHC may likewise be helpful in patients with ductal carcinoma in situ (DCIS). Results from enormous randomized clinical preliminary (NSABP-B24) demonstrated that in quiet with DCIS oversaw by lumpectomy and postoperative radiation, the utilization of

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Tamoxifen brought about an extra half relative decrease in nearby repeats in ER-α positive disease.[5]

It is regularly surveyed by IHC in IBC's. Trama center α manages articulation of PgR, thus the presence of PgR ordinarily demonstrates that the estrogen ER-α pathway is flawless and useful. When communicated PgR is initiated by hormone progesterone to help control a few significant ordinary cell capacities, including multiplication which is inconvenient in bosom cancer.[2]

PgR was estimated by normalized LBA's for almost twenty years and demonstrated to be a powerless prognostic factor yet a moderately solid prescient factor for reaction to hormonal treatment. LBA's for PgR were supplanted by IHC in 1990 and was in the long run affirmed by College of American Pathologists (CAP) and American Society of Clinical Oncologist (ASCO)

PgR is communicated in cores of 60-70% IBCs and their demeanor shifts on a continum going from 0 to almost 100% positive cells, that there is an immediate connection between's PgR levels and reaction to hormonal treatments and that tumor with even extremely low degrees of PgR-positive cells ($\geq$1%) have a noteworthy possibility of responding.[6]

In spite of the fact that the outflow of PgR is profoundly connected with ER-α, the relationship is blemished, bringing about four potential aggregates of joined articulation, each with altogether various paces of reaction to hormonal treatment, which would not be obvious estimating either alone.

In ongoing correlation of patients accepting adjuvant Tamoxifen treatment, the general danger of malady repeats was 28% higher in patients with ER-α-positive/PR-negative than in ER positive/PR positive.[7]

Recognizing these altogether various results is the essential explanation that ER, PR assessment is valuable for choosing treatments.

Presently it has been recommended that practical ER-α which is overwhelmingly atomic in area in most IBC's may likewise dwell at the external cell layer in subset of tumors, particularly those that are HER-2 positive. HER-2 positive IBC and furthermore PgR negative recommend that the atomic ER-α might be non-useful. Anyway film ER-α seems to stay utilitarian & promotes tumor cell expansion in co-activity with over-communicated HER212.

2. Materials and Methods

The present study entitled "Correlation of ER & PR with proto-oncogene & grades of invasive duct carcinoma" was conducted in Dept. of Pathology, at SRMSIMS, Bareilly.

This case study was prospective and retrospective. Prospective cases were selected from the patients admitted for surgery of invasive ductal carcinoma breast in Medical College Hospital. As regards retrospective cases, they were obtained from the histopathological records obtained from Pathology department of SRMS-IMS, Bareilly.

1. Biopsies and mastectomy specimens were fixed in 10% formalin.
2. Detailed history about age, family history, clinical diagnosis and chief complaints was enquired.
3. Tissue was fixed in buffered formalin for about 6 hour after adequate slicing.
4. Gross appearance of mastectomy specimen/biopsy was noted.
5. Paraffin blocks after thorough tissue processing were prepared.
6. Sections were cut 3-4 micron thick and subjected to following:
7. Routine haematoxylin and eosin staining was done for histological typing and grading of all cases.
8. Immunohistochemistry was done using labelled antibodies for hormone receptor status (Oestrogen receptor & Progesterone status), Her2/neu & proliferative index Ki-67.

Invasive ductal carcinomas and all other invasive tumours were graded based on an assessment of tubule/gland formations, nuclear pleomorphism, and mitotic counts as per criteria of Nottingham's grading.

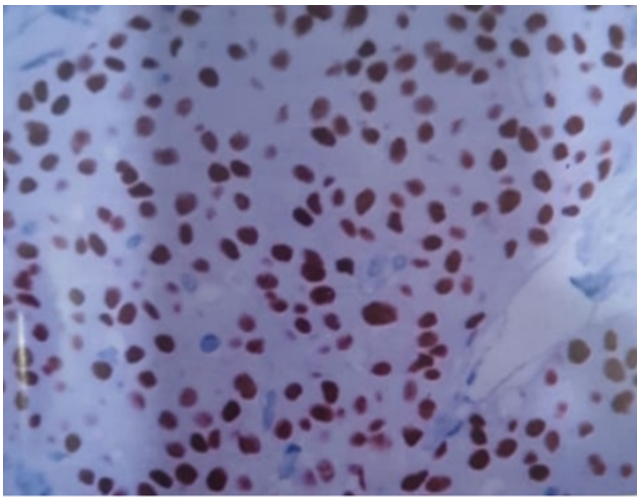


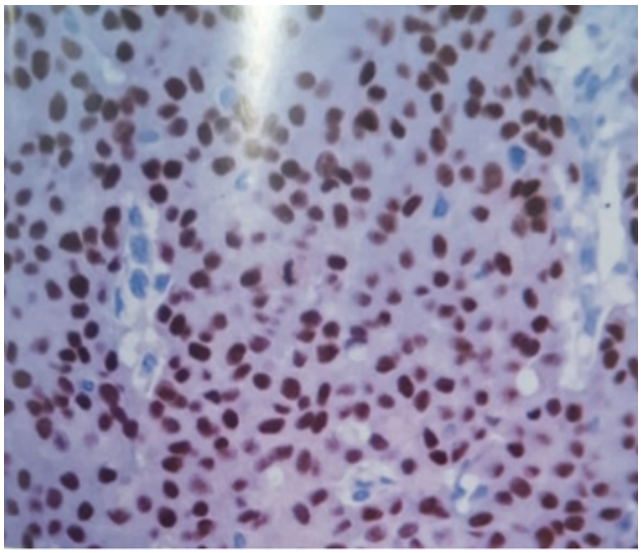
Fig. 1: Positive Control for ER

3. Results

All of the cases were of female, no single case in male was included in study.

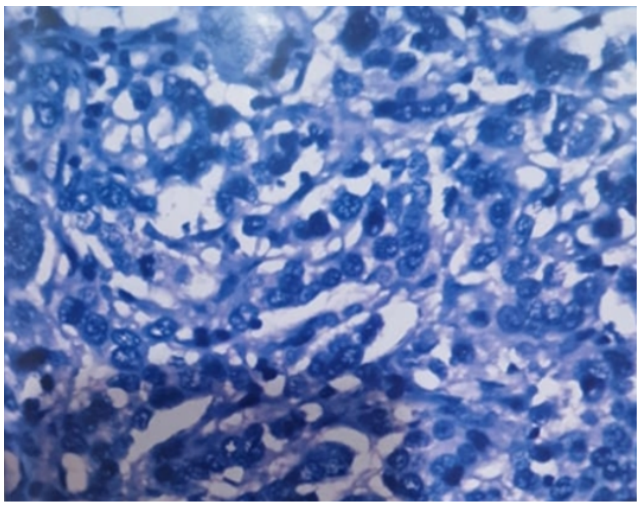
Table 1 Out of 56 cases maximum cases (53.5%) were in the age group of 41-50 years followed by (21.4%) of age group 51-60 years. The youngest patient was 37 years in age and the oldest was 68 years old.

All of the cases were of female, no single case in male was included in study.



5-Positive control for PR

Fig. 2: Positive Control for PR



6-Negative control

Fig. 3: Negative Control

Table 1: Age –wise distribution of cases

Age(in years)	Number of cases	Percentage
0-10	-	-
11-20	-	-
21-30	-	-
31-40	06	10.7%
41-50	30	53.5%
51-60	12	21.4%
>60	08	14.28%

Table 2: Distribution of cases according to quick score

Quick Score	ER		PR	
	No. of cases	Percentage	No. of cases	Percentage
0	24	42.85	22	39.28
2	-	-	-	-
3	10	17.85%	08	14.28%
4	-	-	06	10.71%
5	06	10.71%	06	10.71%
6	07	12.50%	05	8.92%
7	04	7.14%	02	3.57%
8	05	8.92%	07	12.5%

Table 3: Correlation of ER/PR status with grade of tumour

Grade of Tumor	ER Positive	PR Positive	ER Negative	PR Negative
1(7)	05	05	02	02
2(39)	25	28	14	11
3(10)	02	01	08	09

The quick scoring of ER & PR is combination of proportion and intensity scoring. Out of 56 cases, 24 cases (42.85%) were ER negative & 22 cases (39.28%) were PR negative while both were negative in 18 cases (32.14%).

There was a significant relationship between tumour grading & receptor status. As the grade of tumour increases ER & PR positivity decreases. Most of the tumour of grade 1 were both ER & PR positive.

Here the value of ($p<0.05$) for both ER & PR which is significant.

4. Discussion

For all invasive carcinomas, hormone receptor status was also studied using immunoperoxidase method and quick scoring was done.

The Quick score for ER was 0 in 42.85% (24/56) cases & for PR was 0 in 39.28% (22/56) cases, signifying no hormone expression in the majority. Only 32.6% of tumors were ER positive & 46.1% were PR positive in Indian population as compared to high rates 23. Among the 56 cases studied, 57.14% cases were positive for ER & 60.71% cases were positive for PR. In accordance with the study of Lakmini & Mudduwa,[8] in which out of 151 breast cancer patients studied, the Quick score for ER was 0 in 54.3%(82/151) cases & for PR was 0in 51.7% (75/ 145) cases. Desai et al in their study document the ER & PR status of breast cancer in Indian population.[9]

Both ER and PR positive immunostaining was seen in 71.42%cases of evaluation I 64.10% of evaluation II were discovered ER positive and 71.79% were discovered PR positive and 20% instances of evaluation III were discovered ER positive and 10% were discovered PR positive.

The ER & PR positive was highest in grade I lesions followed by grade II lesions & grade III lesions. On statistical analysis there was an inverse high correlation (P<0.05) between hormone receptor immunoreactivity and histological grading.

These findings were in accordance with the study of Bu on who performed a study on 80 invasive breast carcinomas to evaluate the immunohistochemical analysis of estrogen receptor (ER) and progesterone receptor (PR) in invasive breast carcinomas of various histological subtypes and grades. Positive immunoreactivity for ER and PR were seen in 71.25% and 60.00% cases, separately. Both ER and PR positive immunostaining was seen taking all things together (100%) very much separated (grade I) bosom carcinomas, while in grade II tumors ER and PR-positive malignancy cells were 76.36% and 61.62%, individually. The relating figures for grade III carcinomas were 41.18% and 35.29%. A significant association (P<0.05) between different histological grades of breast carcinomas and ER and PR immunore activity was found. Moreover, our findings, showed that ER and PR positivity declined with increasing tumor grade.

However, the current study enforces a fact documented in previous studies that the overall hormone positivity in India is low. The ER expression in our patient population in the best possible situation was 50.5% & the PR expression was 42% as opposed to the 75% ER & 58% PR positivity reported in the literature.[10] The chief cause for false negativity in hormone receptor demonstration by immunohistochemistry is improper fixation leading to inefficient retrieval.[11] This could be also the reason for lower rates of ER/PR positivity in our study too.

5. Conclusion

For all invasive carcinomas, hormone receptor status is also studied using immunoperoxidase method & Quick scoring was done with ER was 0 in 42.85% (24/56) cases & for PR was 0 in 39.28% (22/56) cases, indicating no hormone expression in majority. Among the 56 cases studied, 57.14% cases were positive for ER & 60.71% cases were positive for PR.

Hormone receptor status was also correlated with other tumor characteristics as histological grading. Both ER & PR positive immune staining was observed in 71.42% cases of grade I, 64.10% casesof grade II were positive for ER & 25% were positive for PR & 20% cases of grade III were found positive for ER & 10% was found positive for PR.

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No financial support was received for the work within this manuscript.

7. Conflict of Interest

The authors declare they have no conflict of interest.

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