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A Study on Hormone Receptor Status in Breast Cancer In Relation To Histological Grading, Age and Lymph Node Involvement

1.Dr.R. Rani Suganya, 2.Dr.M. Annapoorani, 3.Dr.C. Naveen Kumar,
*M.S., Assistant Professor, Dept. Of General Surgery, Govt. Stanley Medical College, Chennai – 1**
M.S., Assistant Professor, Govt.Kilpauk Medical College, Chennai-1
Post Graduate, Dept. Of General Surgery, Govt. Stanley Medical College, Chennai-1

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ABSTRACT: Breast cancer is the major health problem for the women throughout the world.
Management of breast cancer has evolved to include both surgery for local disease and medical therapy for systemic disease. Multiple treatment options are available depending on various factors such as histological grade, hormone receptor status etc. The aim of this study is to correlate the hormone receptor status with prognostic factors such as lymph node involvement, tumour grading and age among patients diagnosed with breast cancer in our institution. The results of this study serve to prognosticate the severity of disease among various strata of patients.

KEYWORDS: Carcinoma Breast, Stanley, Estrogen receptor, Progesterone receptor, HER-2/Neu.

I. INTRODUCTION:

Breast cancer accounts for 33% of all female cancers and 20% of cancer related deaths in women. Every year 9,00,000 new cases are diagnosed and causes approximately 3,76,000 deaths annually worldwide.

In Chennai breast cancer accounts for 26.8% of all cancers in women. A few decades back breast carcinoma is more common in women above 50 years comprising about 65% to 70% with 30% to 35% of women were below 50 years of age. But at present the scenario has changed with increasing incidence below 50 years of age comprising of about 49%. Breast cancer scenario in India also shows a significant trend of increased incidence of breast cancer in much younger age than earlier.

Current treatment strategies take into account tumour cells, size and location of the tumour to guide treatment. At present, there are choices of conservative and reconstructive surgery which is more popular than mastectomy due to the availability of increased range of systemic, cytotoxic and hormonal drugs used in neoadjuvant and adjuvant settings.

Prognosis and management of breast carcinoma depends upon the histological type, grade, tumour size, nodal status, hormonal receptor status and HER-2/neu overexpression.

Identification of biomarkers plays an important role in the prognosis and management of breast carcinoma. At the time of diagnosis, determination of hormonal status forms an important step in primary assessment. Identification of Estrogen and Progesterone receptor at the time of diagnosis plays a crucial role to plan for optimal treatment of breast carcinoma.

Estrogen exposure is a well-established predictive and prognostic factor for developing ER-positive breast cancer. Estrogen is a steroid hormone. It has a proliferative effect on normal human mammary epithelium through its activation of Estrogen receptor, a nuclear hormone receptor. ER positivity is overexpressed in as many as 70% of breast cancers. Today, Estrogen receptor remains a very effective target for breast cancer treatment. ER/PR-positive tumours have a better prognosis than ER/PR-negative tumours. Hormone receptor test is done routinely since hormone treatment has fewer side effects and it prevents recurrence in about 25% of cases.

HER2 amplification or protein overexpression is associated with accelerated cell growth and proliferation. It is also associated with an increased risk of recurrence and shortened overall patient survival. The prognosis of HER-2/neu positive tumours are worse than HER2/neu negative tumours. It serves as a marker of aggressive disease and a biologic target for treatment. It is sensitive to treatment with monoclonal antibody Trastuzumab (Herceptin).

II. OBJECTIVES:

The aim of this study is to

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a) Correlate ER, PR and HER 2/Neu receptor status with lymph node, tumour grading and age of the patient.
b) Evaluate the occurrence of histological variants of carcinoma breast in patients attending OPD in Govt. Stanley Medical College Hospital.

III. METHODS:

This is an analytical study done during the period from January 2019 to October 2019. It is conducted among female patients who presented with a breast lump in the female OPD, The Department of General surgery, Govt. Stanley Hospital, Chennai.

Female patients with palpable lump are admitted and are subjected to detailed history regarding age, parity, family history, socio economic status, menstrual history, lactational history and any previous biopsy reports if any.

Based on the clinical examination, patients are subjected to mammogram and Core needle biopsy.Based on the results, if proven malignant, staging workup done with Chest Radiograph, Ultrasonogram Abdomen and Bone scan (LABC).Based on the above findings patients are categorised as

1. Early Breast carcinoma (T1, T2, N1, N0).
2. Locally Advanced Breast Carcinoma (TxN2, T3Nx, T4Nx)

In Early breast cancer patient is subjected to MRM. The specimen is sent for histopathological study and hormone receptor study. Based on the histopathological report and hormone receptor status, patient is followed up with adjuvant chemotherapy and radiotherapy.

In Locally advanced breast carcinoma patient is subjected to core needle biopsy and the specimen is sent for histopathological study and hormone receptor status.Based on the report patient is started on neoadjuvant chemotherapy followed by MRM. Postoperatively patient is started with chemotherapy/radiotherapy Immunohistochemical analysis of hormone receptors are done in formalin fixed paraffin wax embedded tissue sections using the Supersensitive Polymer HRP system which is based on non- biotin polymeric technology.

IV. OBSERVATION AND RESULTS:

A total of 50 patients who were diagnosed with carcinoma breast were operated during the study period.

Table 1: Age wise distribution

S.NO.	AGE (IN YEARS)	CARCINOMA BREAST PATIENTS
1	Less than 20	0
2	21 – 30	3
3	31 – 40	7
4	41 – 50	21
5	51 – 60	14
6	More than 60	5
TOTAL		50

Table 1 shows the distribution of breast tumours according to age. Carcinoma Breast had a peak incidence in the age group of 41 – 50 years.

Table 2. Distribution of histological variants in breast carcinoma

S.NO	HISTOLOGICAL VARIANTS	NO. OF CASES	PERCENTAGE
1	Invasive Ductal Carcinoma-NOS type	47	94%
2	Invasive Lobular Carcinoma	2	4%
3	Mucinous Carcinoma	1	2%
TOTAL		50	100%

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Table 2 shows the distribution of histological variants in breast carcinoma. Among the 50 cases, 47 cases (94%) were Invasive Ductal Carcinoma NOS type, 2(4%) were Invasive Lobular carcinoma and 1 (2%) was Mucinous carcinoma.

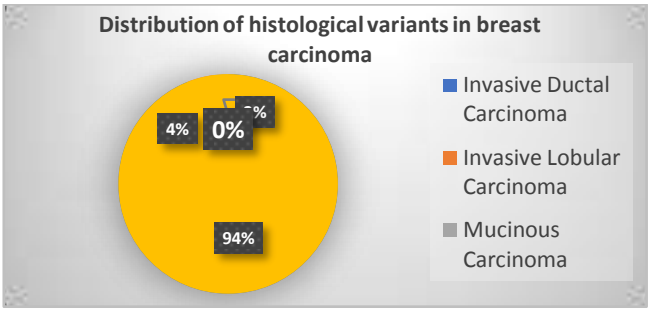

Table 3. Distribution of histological grade in invasive ductal carcinoma –NOS type.

S.NO	HISTOLOGICAL GRADE	NO. OF CASES	PERCENTAGE
1	GRADE I	8	17 %
2	GRADE II	33	70 %
3	GRADE III	6	12 %
TOTAL		47	100 %

Table 3 shows the distribution of histological grading in breast carcinoma according to Modified Bloom Richardson scoring system. Only 47 cases were included for grading, in that 8 (17%) cases were in grade I; 33 cases (70%) were in Grade II, 6 cases (13%) were in Grade III.

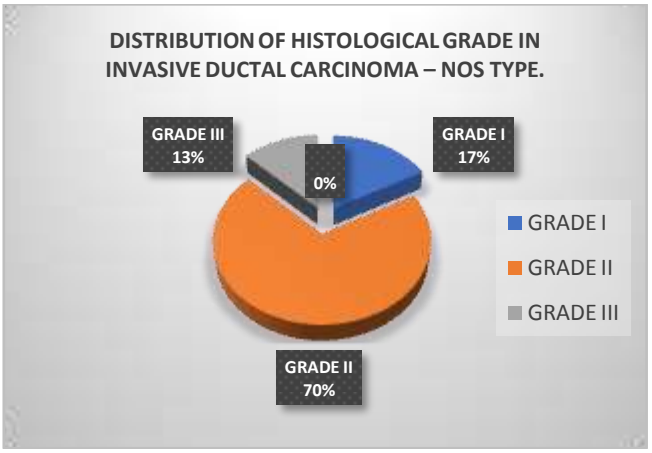

Table 4. Correlation of Estrogen receptor with progesterone receptor.

S.NO	GROUP	NO. OF CASES	PERCENTAGE
1	ER+/PR+	22	44 %
2	ER-/PR+	09	18 %
3	ER+/PR-	04	8 %
4	ER-/PR-	15	30%
TOTAL		50	100 %

Table 4. shows correlation of Estrogen receptors and Progesterone receptors. Among the 50 cases 22 cases were positive for both Estrogen and Progesterone receptors, 9 cases positive for progesterone receptor, 4 cases positive for Estrogen receptor, while 15 cases were negative for both estrogen and progesterone receptors.

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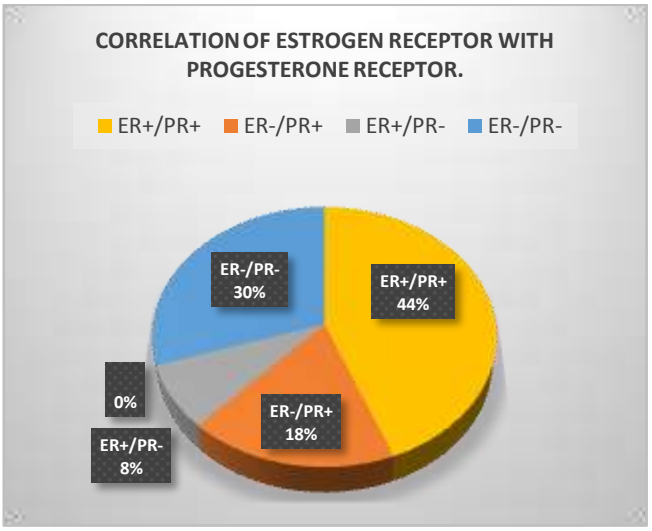

Table 5. Expression of HER-2/neu in breast carcinoma

S.NO	HER-2/Neu EXPRESSION	TOTAL NO. OF CASES	PERCENTAGE
1	POSITIVE	50	36%
2	NEGATIVE		64%

Table 5. shows HER-2/neu overexpression in 50 cases of breast carcinoma, among them 18 cases (36%) were found to be positive, while 32 cases (64%) were found to be negative.

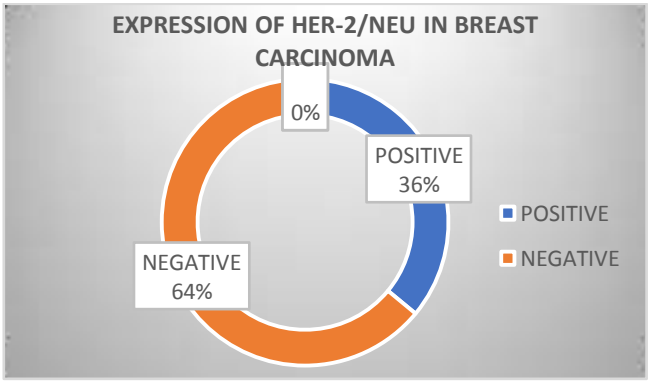

Table 6. Correlation of tumour size with hormone receptors

S.NO	TUMOUR SIZE	TOTAL	ER/PR POSITIVE	PERCENTAGE
1	T_1< 2 cm	7	6	85%
2	T_2 2 – 5 cm	17	16	94%
3	T_3>5 cm	26	13	50%
TOTAL		50	35	

Table 6. shows correlation of hormone receptors with tumour size. Estrogen receptor and Progesterone receptor positivity was noted in 85% of T1 sized tumours, 94% of T2 sized tumours and 50% of T3 sized tumours. The receptor status was found to be comparatively reduced in larger sized tumours as depicted. The correlation of hormone receptor with tumour size was statistically found to be significant (p=0.003).

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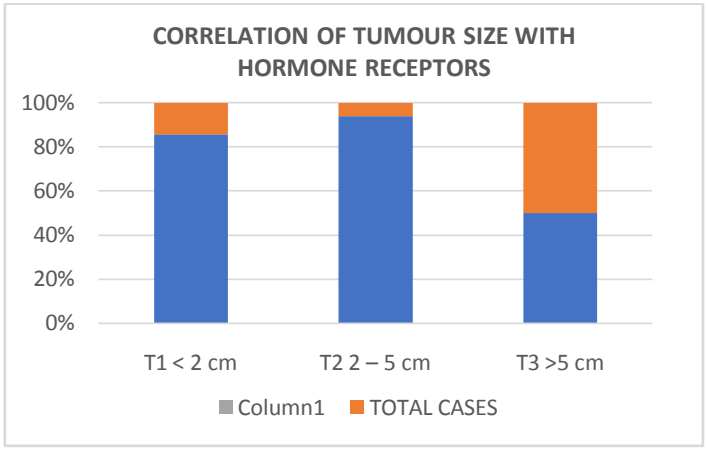

Table 7. Correlation of HER-2/neu with tumour size

S.NO	TUMOUR SIZE	HER-2/Neu POSITIVE	TOTAL CASES	PERCENTAGE
1	<2 cm	1	7	14%
2	2 – 5 cm	5	17	23%
3	>5 cm	14	26	53%

Table 7. shows correlation of HER-2/neu with tumour size. HER-2/neu overexpression was noted in 14% of T1 sized tumour, 23% in T2 sized tumour and 53% in T3 sized tumour. HER-2/neu overexpression was found in increasing size of the tumour.

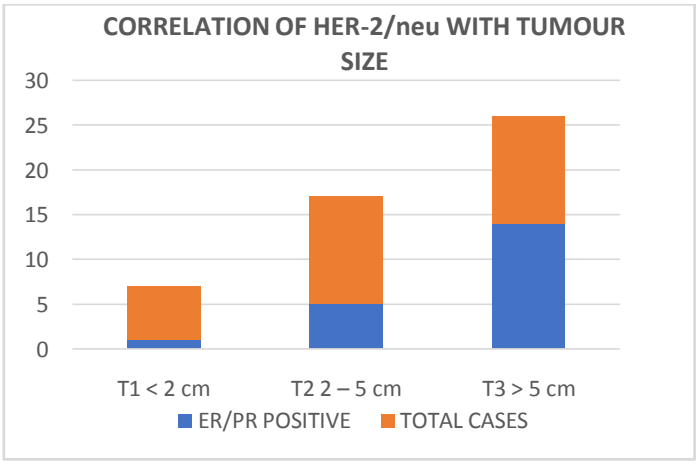

Table 8. Correlation of receptor status with histological grading

S.NO	HISTOLOGICAL GRADE	TOTAL NO. OF CASES	ER/PR +VE	PERCENTAGE
1	GRADE I	8	8	100%
2	GRADE II	33	23	69%
3	GRADE III	6	2	33%

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Table 8. shows correlation of hormone receptor status with tumour grade. Estrogen, Progesterone receptor positivity was seen in 100% in grade I tumours, 69% in grade II tumours and 33% in grade III tumours. This implies that high histological grade tumours showed low expression of tumours.

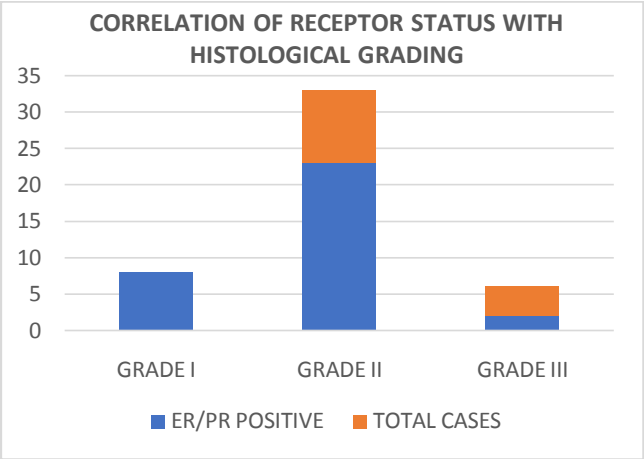

Table 9. Correlation of her-2/neu with histological grading

S.NO	HISTOLOGICAL GRADE	HER-2/neu POSITIVE	PERCENTAGE
1	GRADE I (8 CASES)	0	0
2	GRADE II (33 CASES)	11	33%
3	GRADE III (6 CASES)	2	66%

Table 9. shows correlation of HER-2/neu with histological grade. It was found that HER-2/neu overexpression was not seen in grade I tumours, where as it was expressed in 33% of grade II tumours and 66% of grade III tumours. Statistically, found to be significant (p=0.001).

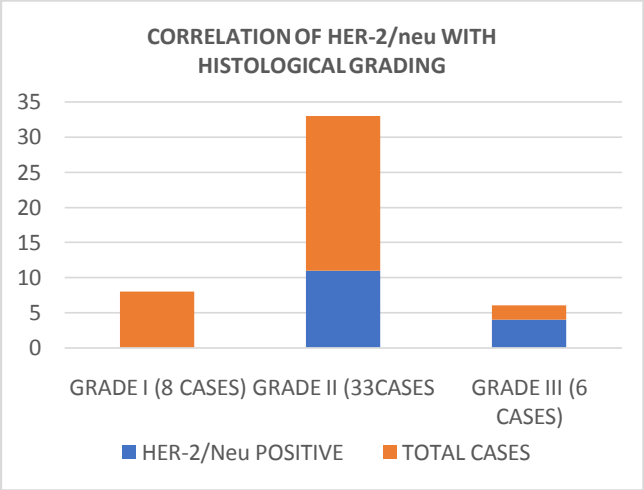

Table 10. Correlation of receptor status with nodal status

S.NO	NODAL METASTASIS	ER/PR POSITIVE	PERCENTAGE
1	PRESENT (17 CASES)	9	52%

2	NEGATIVE (29 CASES)	21	72%

Table 10. shows correlation of hormone receptors with nodal status. Out of 46 patients 17 had nodal metastasis, among whom 9 showed receptor positivity. Out of 29 nodal negative patients, receptor status was positive in 21 patients. This explains higher receptor expression in nodal negative patients. Statistically found to be significant (p=0.001).

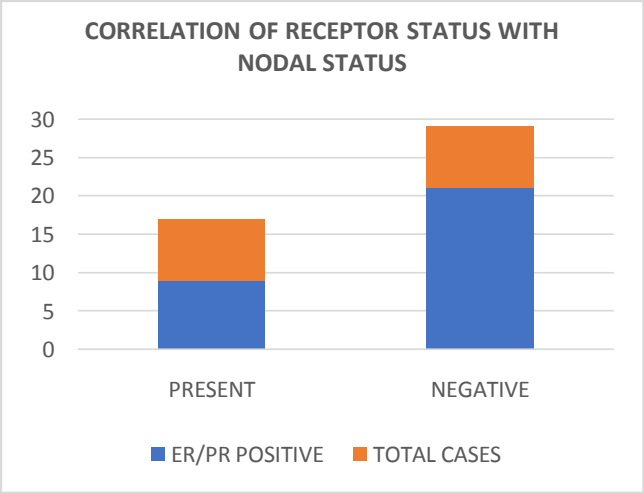

Table 11. Correlation of her-2/neu with nodal status

S.NO	NODAL METASTASIS	HER-2/Neu POSITIVE	PERCENTAGE
1	PRESENT (17 CASES)	11	64%
2	NEGATIVE (29 CASES)	2	6%

Table 11. shows correlation of HER-2/neu with nodal status. Out of 46 cases, HER-2/neu overexpression was seen in 64% of nodal positive patients as opposed to 6% of nodal negative patients. Statistically found to be significant (p=0.001).

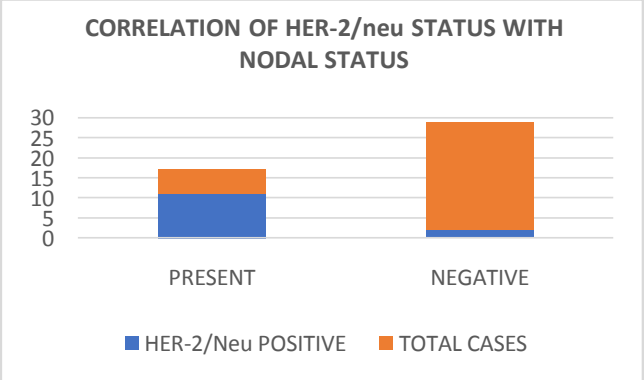

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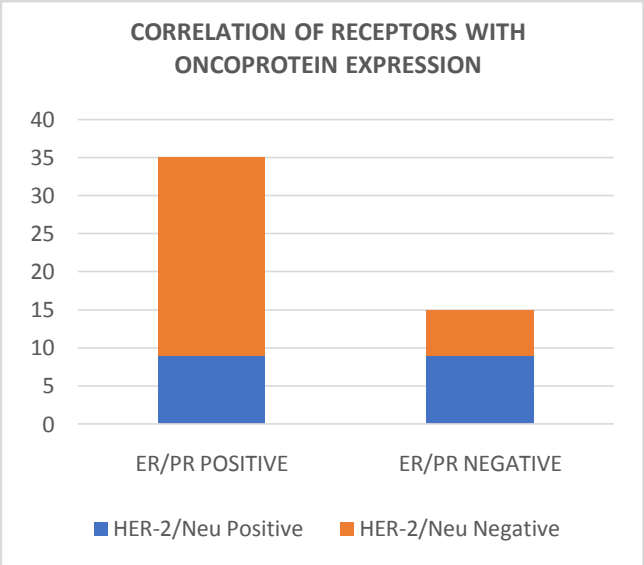
Table 12. Correlation of receptors with oncoprotein expression

ER/PR STATUS	HER-2/Neu		TOTAL NO. OF CASES
	POSITIVE	NEGATIVE	
POSITIVE	9	26	35
NEGATIVE	9	6	15
TOTAL NO. OF CASES	18	32	50

Table 12. shows an inverse relationship of estrogen, Progesterone receptor status with the HER-2/neu status. Statistical analysis was performed and found to significant (p=0.001).



V. DISCUSSION:

HORMONE RECEPTOR STATUS AND HER-2/NEU IN BREAST CARCINOMAS

Estrogen, Progesterone receptor positive tumours have a significantly longer disease-free survival than with the receptor negative tumours. In 1975 Rosen et al. attempted to correlate Estrogen, Progesterone receptors status along with various histological types of breast carcinoma. In his study Estrogen, Progesterone receptors were positive in 70-80% of the tumours and HER-2/ neu expression was positive in 15-20% of the breast carcinoma specimen.

In the present study Estrogen, Progesterone receptor or both were positive in 70% of cases and both receptors were negative in 30% of cases (Tab.5).

HER-2/neu overexpression was positive in 36% of cases (Tab.6). Hence this study is comparable with the studies conducted in the Asian communities. There appears to be a minimal variation in receptor expression; because technically this could be explained by the differences in the technique of evaluation and inter laboratory variations.

Estrogen, Progesterone Receptor And Her-2/Neu Status In Histological Variants

The present study shows Estrogen and Progesterone receptor positivity and HER-2/neu expression negativity among invasive ductal carcinoma. Invasive lobular carcinoma in the current study also expressed both receptors and HER-2/neu negativity. Clinicopathologically this can be explained by the aggressive nature of the tumourwith higher incidence of nodal metastases.

ESTROGEN, PROGESTERONE RECEPTOR, HER-2/NEU WITH OTHER VARIABLES

Current study shows correlation of hormone receptors and HER-2/neu with tumour size. The tumours are categorized into three according to T in TNM staging. T1- < 2cm, T2=2-5cm, T3 = > 5 cm. Receptor positivity is expressed in 85% of T1, 94% of T2 and 50% of T3 tumours.

This explains that receptor positivity has an inverse relationship with the tumour size.

HER-2/neu overexpression showed positivity in 14% of T1,23% in T2 and 59% in T3 tumours. This explains the higher expression of oncoprotein among the tumours of more than 2 cm size.

CORRELATION WITH NODAL STATUS

In the present study out of 46 patients 17 cases showed metastasis while 29 cases have no metastases. Receptor positivity was found to be higher among the nodal metastasis negative patients which was about 72% (21/29). HER-2/neu overexpression was seen in 64% of nodal positive cases than the nodal negative patients which was found to be 6 %.

Correlation Of Estrogen, Progesterone Receptor With Her- 2/Neu

The present study showed an inverse relationship between these hormone receptors and oncoprotein expression. This can be explained by the fact that there is cross-linkage between the two pathways of tumour growth.

VI. SUMMARY AND CONCLUSION

- Among the various histological variants in breast carcinoma, Invasive Ductal carcinoma – NOS type constituted about 94% of cases.
- Estrogen, Progesterone receptor positivity and HER-2/neu negativity in Mucinous carcinomas.
- Triple negativity in small group of Invasive lobular carcinoma.
- Regarding the histological grade of breast carcinoma, Grade II tumours were common accounting for 70 %.
- Estrogen and Progesterone receptor or both was found in 70% while 30% were found to be receptor negative.
- HER-2 /neu overexpression was found to be positive in 36% of tumours and it was negative in 64% of tumours.
- Out of the total 50 cases, 26 cases were T3 tumours of more than 5cms in diameter.
- Larger the tumour size lesser is the expression of hormone receptor, whereas smaller sized tumours expressed more receptor positivity. This inverse correlation was statistically significant (P=0.003).
- HER-2/neu overexpression was found in tumours of all size. However, there was no significant correlation between the tumour size and HER-2/neu expression.
- Among the 46 cases, nodal metastasis was found in 17 cases and negative in 29 cases.
- Among the 29 nodal negative patients Estrogen, Progesterone receptor were positive in 21 cases. Thus, there is higher receptor expression in nodal negative patients. This was found to have a significant correlation (P=0.001).
- HER-2/neu overexpression was observed in 64% of nodal positive patients, which is statistically significant (P=0.001).
- Higher the histological grade of breast carcinoma, lower the receptor positivity. 33% of the grade III tumours expressed receptor positivity in comparison to 100% in grade I tumours.
- Higher the histological grade of breast carcinoma, greater the HER-2/neu overexpression, which was found to have a significant correlation (P=0.001).
- Higher the Estrogen, Progesterone receptor positivity, lower was the HER-2/neu overexpression. Thus, there was an inverse relation between the receptor and HER-2/neu, which was found to be statistically significant (P=0.001)

CONCLUSION:

Estrogen, Progesterone receptor positive tumours are more common in the post-menopausal women, tumours of more than 2cm in size, Histological grade I and in nodal negative patients.

Oncoprotein overexpression is common among the tumours of more than 2cm in size, grade III tumours and in nodal positive patients.

Hormone receptor and oncoproteinexpression has an inverse correlation with each other.

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