

STUDY OF HISTOMORPHOLOGY AND IMMUNOHISTOCHEMICAL ANALYSIS IN BREAST NEOPLASMManish Kaushal¹, Arvind Shukla², Pankaj Patil³¹Associate Professor, Department of Surgery, MGMMC and MY Hospital, Indore, Madhya Pradesh.²Assistant Professor, Department of Surgery, MGMMC and MY Hospital, Indore, Madhya Pradesh.³Junior Resident, Department of Surgery, MGMMC and MY Hospital, Indore, Madhya Pradesh.**ABSTRACT****BACKGROUND**

Carcinoma of the breast is the most common malignant tumour and the most common cause of death from carcinoma in females all over the world.⁽¹⁾ The important pathological prognostic factors in invasive breast carcinoma include patient's age, tumour size, lymph node metastasis, nuclear grade, histological grade, histological type, hormone receptor status and HER-2/neu.⁽²⁾ A single parameter with the strongest prognostic significance is hormone receptor status.

Aims and Objectives-

1. Occurrence of ER, PR and HER-2/neu in post-surgical histological specimen.
2. Expression of ER, PR and HER-2/neu receptors as per staging in carcinoma breast.
3. To co-relate histomorphological variants with immunohistochemistry.

MATERIALS AND METHODS

A hospital-based, prospective, observational study was conducted at Department of Surgery, MGM Medical College and MY Hospital, Indore. A total of 50 diagnosed carcinoma breast cases coming to our hospital were taken into study after informed consent. Detailed history was taken from patients and a biopsy specimen was taken from all patients. Gross examination pertaining to overall size of the specimen, nipple and areola, tumour size, margin status and nodal status were carefully studied. The tissue was processed for routine histopathological examination and stained with haematoxylin and eosin. The slides were then stained with ER, PR and HER-2/neu antibodies.

RESULTS

Mean age of the study subjects was 54.32 years, while age at menarche and menopause was 13.12 years and 44.61 years respectively. Most common type of carcinoma seen in the present study was invasive ductal carcinoma (90%). Out of the total 50 cases, 20% and 42% were in stage I and II respectively, while 36% and 2% were in stage III and IV. Prevalence of positive oestrogen receptor, progesterone receptor and HER-2/neu status was seen in 52%, 48% and 24% cases respectively. No association was observed between age at diagnosis and parity with positive hormonal status. A significant association was observed between increasing tumour size and LN status with positive HER-2/neu and ER and PR negative status ($p < 0.05$). Out of the 19 cases of stage III/IV approx. 31.6% are ER and PR+, while out of 31 cases in stage I/II 64.5% were ER and PR positive ($p < 0.01$). Similarly, 22.6% cases of stage I/II were HER-2/neu positive as compared to 21.05% of stage III and IV ($p=0.27$).

CONCLUSION

The frequency of carcinoma of breast is high in post-menopausal group. The most common tumour pathology found in the study was Ductal Carcinoma. Definitive prognostic correlation was found with ER and PR receptors. HER-2/neu expression was high in advanced diseases like axillary node positive patients. The clinical importance of these prognostic markers in the management of breast cancer in clinical practice is strongly recommended.

KEYWORDS

ER, PR, HER-2/NEU.

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BACKGROUND

Carcinoma of the breast is the most common malignant tumour and the most common cause of death from carcinoma in females all over the world.

The important pathological prognostic factors in invasive breast carcinoma include patient's age, tumour size, lymph node metastasis, nuclear grade, histological grade,

histological type, hormone receptor status and HER-2/neu. A single parameter with the strongest prognostic significance is hormone receptor status.⁽³⁾ Intracellular steroid-hormone receptor proteins, primarily oestrogen receptor (ER) and progesterone receptor (PR) have received intensive study, both as indicator of prognosis and as guide to hormone therapy.⁽⁴⁾

The present study was thus aimed to evaluate the prevalence and to understand the role of ER, PR and HER-2 status in choice of treatment for further management in patients of breast carcinoma.

MATERIALS AND METHODS

A hospital-based prospective observational study was conducted at Department of Surgery, MGM Medical College and MY Hospital, Indore. A total of 50 diagnosed carcinoma

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breast cases coming to our hospital were taken into study after informed consent. Detailed history was taken from patients and a biopsy specimen was taken from all patients. Gross examination pertaining to overall size of the specimen, nipple and areola, tumour size, margin status and nodal status were carefully studied. The tissue was processed for routine histopathological examination and stained with Haematoxylin and eosin. The slides were then stained with ER, PR and HER-2/neu antibodies.

Statistical Methods Applied

Data were statistically described in terms of mean (\pm SD), frequencies (number of cases) and percentages when appropriate. Data were tested first for normal distribution by Kolmogorov-Smirnov test. Comparison of quantitative variables between the study groups was done using student's 't' test for independent samples if normally distributed. Mann-Whitney U test was used for non-normally distributed quantitative data. For comparing categorical data, Chi-square test was performed. Exact test was used instead when the expected frequency was less than 5. For qualitative comparison of tables over 2 x 2 dimensions like TNM staging, p-trend value was calculated. A probability value (p value) less than 0.05 was considered statistically significant. All statistical calculations were done using computer programs Microsoft Excel 2007 (Microsoft Corporation, NY, USA) and SPSS (Statistical Package for the Social Sciences, SPSS Inc., Chicago, IL, USA) version 21.

Inclusion Criteria

1. Clinically diagnosed carcinoma breast in females above 30 years of age.
2. Patients who gave written informed consent.

Exclusion Criteria

1. Those who have undergone any chemoreduction treatment.
2. Patients already treated for contralateral breast cancer.
3. Patients not willing to give written consent.

RESULTS

1. Mean age of the study subjects was 54.32 years, while age at menarche and menopause was 13.12 years and 44.61 years respectively.
2. Most common type of carcinoma seen in present study was invasive ductal carcinoma (90%).
3. Out of the total 50 cases 20% and 42% were in stage I and II respectively, while 36% and 2% were in stage III and IV.
4. Prevalence of positive oestrogen receptor, progesterone receptor and HER-2/neu status was seen in 52%, 48% and 24% cases respectively.
5. No association was observed between age at diagnosis and parity with positive hormonal status.
6. A significant association was observed between increasing tumour size and LN status with positive HER-2/neu and ER and PR negative status ($p < 0.05$).
7. Out of 19 cases of stage III/ IV, approx. 31.6% are ER and PR+, while out of 31 cases in stage I/II 64.5% were ER and PR positive ($p < 0.01$). Similarly, 22.6% cases of stage I/II

were HER-2/neu positive as compared to 21.05% of stage III and IV ($p=0.27$).

DISCUSSION

A hospital-based prospective observational study was conducted at Dept. of Surgery of a tertiary care hospital with the objective of finding the correlation of ER, PR and HER-2/neu incidence with other prognostic factors like age, parity, tumour size and lymph node status. A total of 50 operated cases of carcinoma breast who fulfilled the selection criteria and gave voluntary consent to be a part of the study were enrolled in this study. Following observations were made during the study-

1. Over half of the study subjects (60%) were between 40 - 60 years of age, while 12% were below 40 years of age.
2. Mean age of the study subjects was 54.32 years, while age at menarche and menopause was 13.12 years and 44.61 years respectively.
3. Most of the cases were multipara (94%).
4. About three-fourth of the study subjects belonged to post-menopausal, while 16% were pre-menopausal.
5. Family history of carcinoma breast to first-degree relative was given by 18% cases.
6. Both sides were equally involved in the present study. No case of bilateral carcinoma was seen in our study.
7. Most common type of carcinoma seen in the present study was Invasive ductal carcinoma (90%). Other cases were of malignant phyllodes (4%), mucinous carcinoma (4%) and papillary carcinoma (2%).
8. About half of the cases were in "T" stage 2, while lymph node involvement was seen in 42% cases. Metastasis was observed in 2% cases.
9. Out of the total 50 cases 20% and 42% were in stage I and II respectively, while 36% and 2% were in stage III and IV.
10. Prevalence of positive oestrogen receptor, progesterone receptor and HER-2/neu status was seen in 52%, 48% and 24% cases respectively.
11. No association was observed between age at diagnosis and positive oestrogen receptor, progesterone receptor and HER-2/neu status ($p > 0.05$).
12. No association was observed between parity and positive oestrogen receptor, progesterone receptor and HER-2/neu status ($p > 0.05$).
13. A significant association was observed between increasing tumour size with positive HER-2/neu positive status and ER and PR negative status ($p < 0.05$).
14. Out of 29 cases with negative lymph node status, positive oestrogen and progesterone receptor status was seen in 19 (65.5%) and 17 (58.6%), while out of 21 cases with positive LN status 66.7% each were ER and PR negative ($p < 0.05$). Similarly, out of the 29 cases with negative lymph node status 86.2% were HER-2/neu negative and out of 21 positive cases, 38.1% were HER-2/neu positive ($p < 0.05$).
15. Out of the 19 cases of stage III/ IV approx. 31.6% are ER and PR+, while out of 31 cases in stage I/II 64.5% were ER and PR positive ($p < 0.01$). Similarly, 22.6% cases of stage I/II were HER-2/neu positive as compared to 21.05% of stage III and IV ($p=0.27$).

Age at Diagnosis (Yrs.)					
Variables	Results	N	Mean	SD	P-value
ER	Negative	24	53.58	10.23	0.54
	Positive	26	54.90	11.57	
PR	Negative	26	54.68	11.93	0.69
	Positive	24	53.81	9.75	
HER-2/Neu	Negative	38	54.91	11.58	0.3
	Positive	12	52.25	8.35	

Table 1. Association of Hormonal Receptors with Age at Presentation

No association was observed between age at diagnosis and positive oestrogen receptor, progesterone receptor and HER-2/neu status (p > 0.05).

Age at Menarche (Yrs.)					
Variables	Results	N	Mean	SD	P-value
ER	Negative	24	13.43	3.23	0.79
	Positive	26	13.01	3.10	
PR	Negative	26	12.96	2.39	0.61
	Positive	24	13.38	3.65	
HER-2/Neu	Negative	38	13.21	3.54	0.48
	Positive	12	12.49	2.44	

Table 2. Association of Hormonal Receptors with Age at Menarche

No association was observed between age at menarche and positive oestrogen receptor, progesterone receptor and HER-2/neu status (p > 0.05).

Age at Menopause (Yrs.)					
Variables	Results	N	Mean	SD	P-value
ER	Negative	24	44.58	5.18	0.891
	Positive	26	44.79	5.56	
PR	Negative	26	44.12	5.09	0.67
	Positive	24	44.91	5.77	
HER-2/Neu	Negative	38	44.77	5.91	0.59
	Positive	12	43.81	5.32	

Table 3. Association of Hormonal Receptors with Age at Menopause

No association was observed between age of menopause and positive oestrogen receptor, progesterone receptor and HER-2/neu status (p > 0.05).

Parity	ER		PR		HER-2/NEU	
	Negative	Positive	Negative	Positive	Negative	Positive
Multi	22	25	24	23	35	12
	46.8%	53.2%	51.1%	48.9%	74.5%	25.5%
Primi	2	1	2	1	3	0
	66.7%	33.3%	66.7%	33.3%	100.0%	0.0%
Total	24	26	26	24	38	12
P-value	0.345		0.489		0.664	

Table 4. Association of Hormonal Receptors with Parity

No association was observed between parity and positive oestrogen receptor, progesterone receptor and HER-2/neu status (p > 0.05) and HER-2/neu status (p > 0.05).

Tumour Size (TNM)	ER		PR		HER-2/Neu	
	Negative	Positive	Negative	Positive	Negative	Positive
0	0	3	1	2	3	0
	0.0%	100.0%	33.3%	66.7%	100.0%	0.0%
1	2	5	2	5	7	0
	28.6%	71.4%	28.6%	71.4%	100.0%	0.0%
2	11	15	12	14	22	4
	42.3%	57.7%	46.2%	53.8%	84.6%	15.4%
3	3	1	3	1	2	2
	75.0%	25.0%	75.0%	25.0%	50.0%	50.0%
4	8	2	8	2	4	6
	80.0%	20.0%	80.0%	20.0%	40.0%	60.0%
Total	24	26	26	24	38	11
P-value	<0.05		<0.05		<0.05	

Table 5. Association of Hormonal Receptors with Tumour Size

A significant association was observed between increasing tumour size with positive HER-2/neu positive status and ER and PR negative status (p < 0.05).

Lymph Node Status	ER		PR		HER-2/Neu	
	Negative	Positive	Negative	Positive	Negative	Positive
Negative	10	19	12	17	25	4
	34.5%	65.5%	41.4%	58.6%	86.2%	13.8%
Positive	14	7	14	7	13	8
	66.7%	33.3%	66.7%	33.3%	61.9%	38.1%
Total	24	26	26	24	38	12
P-value	<0.01		<0.05		<0.05	

Table 6. Association of Hormonal Receptors with Lymph Node Involvement

Out of 29 cases with negative lymph node status, positive oestrogen and progesterone receptor status was seen in 19 (65.5%) and 17 (58.6%), while out of 21 cases with positive LN status (66.7%) each were ER and PR negative (p < 0.05). Similarly, out of 29 cases with negative lymph node status, 86.2% were HER-2/neu negative and out of 21 positive cases 38.1% were HER-2/neu positive (p < 0.05).

TNM Stage	ER		PR		HER-2/Neu	
	Negative	Positive	Negative	Positive	Negative	Positive
I	6	4	7	3	8	2
	60.0%	40.0%	70.0%	30.0%	80.0%	20.0%
II	5	16	6	15	16	5
	23.8%	76.2%	28.6%	71.4%	76.2%	23.8%
III	12	6	12	6	15	3
	66.7%	33.3%	66.7%	33.3%	83.3%	16.7%
IV	1	0	1	0	0	1
	100.0%	0.0%	100.0%	0.0%	0.0%	100.0%
Total	24	26	26	24	39	11
P-value	<0.01		<0.01		0.27	

Table 7. Association of Hormonal Receptors with TNM Staging

Out of the 19 cases of stage III/IV approx. 31.6% are ER and PR+, while out of 31 cases in stage I/II 64.5% were ER and PR positive (p < 0.01).

CONCLUSION

The frequency of carcinoma of breast is high in post-menopausal group. The most common tumour pathology found in the study was Ductal Carcinoma. Definitive prognostic correlation was found with ER and PR receptors.

HER-2/neu expression was high in advanced diseases like axillary node positive patients.^(5,6) The clinical importance of these prognostic markers in the management of breast cancer in clinical practice is strongly recommended.

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