Original Research Article

Correlation of histologic grade of breast carcinoma with hormone receptor status in a tertiary care hospital

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ABSTRACT

Background: Breast cancer is one of the most common malignancies affecting the female population worldwide. Prognosis and management of breast cancer are influenced by variables such as stage, grade, hormone receptor status of oestrogen(ER), progesterone(PR) and Human epidermal growth factor receptor2 (HER2/neu) overexpression. Aim to correlate grade of tumour with ER, PR and HER2/neu receptor status of breast carcinoma.

Methods: A prospective study was done in Pathology department, MGM Medical College and Hospital, Aurangabad, Maharashtra for one year. Out of 65 cases studied, 28 cases were biopsy and 37 cases were modified radical mastectomy specimens. All samples were subjected for routine histological examination and immunohistochemical analysis.

Results: Age of patients ranged from 30 to 82 years; 60% of tumours were right sided; 46% were involving upper outer quadrant; 58% were radiologically BI-RADS 4; 46% tumours were histopathologically grade 2 and 90% were invasive breast carcinoma, not otherwise specified. By immunohistochemistry, 60% were ER/PRpositive, 9% HER2/neu positive, 26% triple negative and 5% HER2/neu equivocal. In our study, out of 13 grade 1 tumours, 100% were ER/PRpositive and HER2/neu negative; thus an inverse relationship was found between HER2/neu and ER/PR receptors. Also 70% of triple negative tumours were grade 3 which have an aggressive behaviour compared to other subtypes and were common in premenopausal women.

Conclusions: Assessment of hormone receptors for clinical management of breast cancer patients is strongly advocated to provide prognostic information and best therapeutic options. A significant correlation was observed between hormonal receptor status and the grade of tumour.

Keywords: Breast carcinoma, Oestrogen receptor, Progesterone receptor, Triple negative and HER2/neu

INTRODUCTION

Breast cancer is one of the most common malignancies affecting the female population worldwide.[1] Prognosis and management of breast cancer are influenced by variables such as stage, grade, hormone receptor status of estrogen (ER), progesterone (PR) and Human epidermal growth factor receptor (HER2/neu) over-expression.[2] Majority of the carcinomas arise from the ER positive luminal cells.[3] ER negative carcinomas may arise from ER negative myoepithelial cells or an ER positive precursor that has lost the expression in the process of evolution of cancer.[3] Tumours that express ER and/or PR have a better prognosis and most of them respond well to hormonal therapy.[4]

HER2 proto-oncogene is amplified and/or over expressed in approximately 25% of invasive primary breast cancers.[2] HER2/neu overexpression is associated with poor histologic grade; so also the triple negative breast carcinomas.[2,5] The study was aimed to correlate the histologic grade of tumour with ER, PR and HER2 status.

METHODS

A prospective study was done in the Pathology department, MGM Medical College and Hospital, Aurangabad, Maharashtra for duration of one year. Out of 65 cases studied, 28 were biopsy specimens and 37 were modified radical mastectomy specimens. All samples were subjected for routine histological examination, were stained with Haematoxylin and Eosin (H and E) staining and were reported according to standard protocol. Histological grading of tumour was done according to modified Bloom-Richardson grading system.

Representative sections of tumour and adjacent uninvolved breast tissue (internal control) were further processed for immunohistochemistry using Peroxidase-antiperoxidase (PAP) technique. Sections were taken on positively charged slides. Antigen retrieval was done using EDTA buffer solution at pH 9.0 and slides were stained with monoclonal antibodies obtained from 'BIOGENEX' company. ER (clone EP1), PR (clone EP2), HER2/neu (clone EP3) immunohistochemistry markers were used. ER, PR positivity was interpreted and reported using Allred scoring system which takes into account both intensity of nuclear staining and proportion of immuno-positive tumour cells. ER, PR is considered to be positive if ≥1% of tumour cell nuclei are immunoreactive. HER2/neu positivity was interpreted and reported using ASCO 2007 guidelines (American Society of Cancer Oncology) which takes into account the cytoplasmic membrane staining and the proportion of immuno-positive tumour cells.

RESULTS

In this study, a total of 65 cases were studied within duration of one year. Out of 65 cases studied, 37 were modified radical mastectomy and 28 were biopsy specimens. Majority of the patients belonged to the age group of 41-50 (34%) and were perimenopausal (Figure 1); 60% of tumours were located at the right side, 38% at the left and 2% case were bilateral (Figure 2). Majority of tumours were located in upper outer quadrant (46%) (Figure 3) and 58% cases of breast lumps were reported to be BI-RADS category IV on mammography (Figure 4).
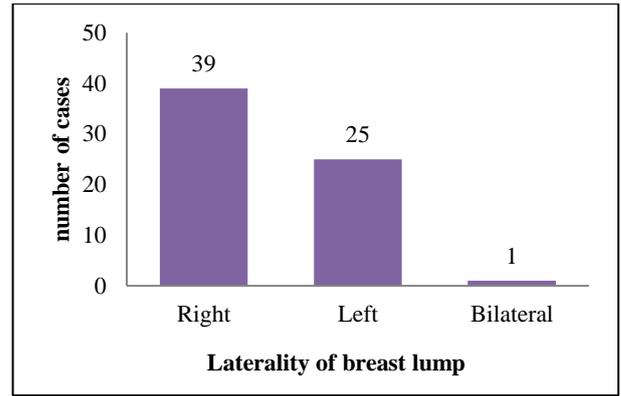

Figure 1: Age distribution.

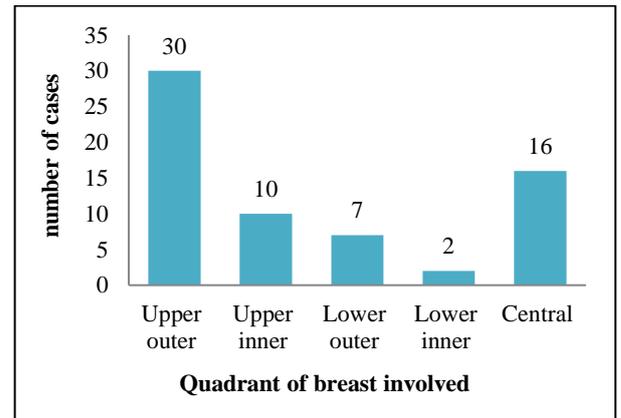

Figure 2: Laterality of breast lump.

Figure 3: Quadrant of breast involved.
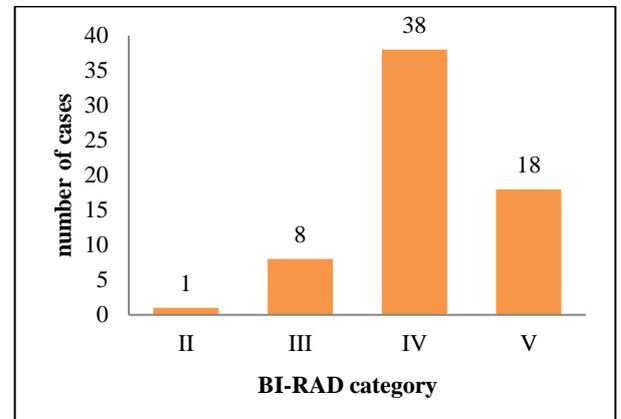
Figure 4: BI-RAD category.
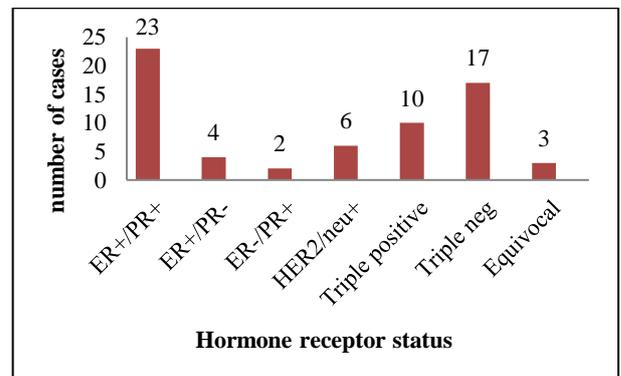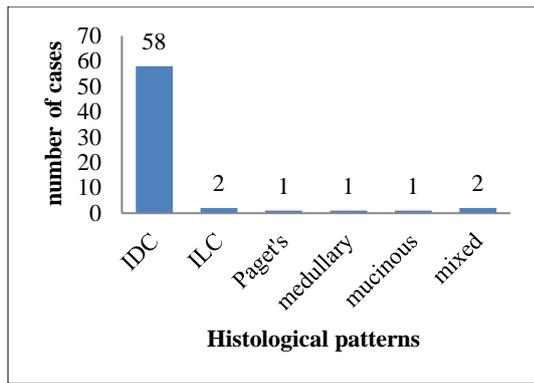

Figure 5: Hormone receptor status.
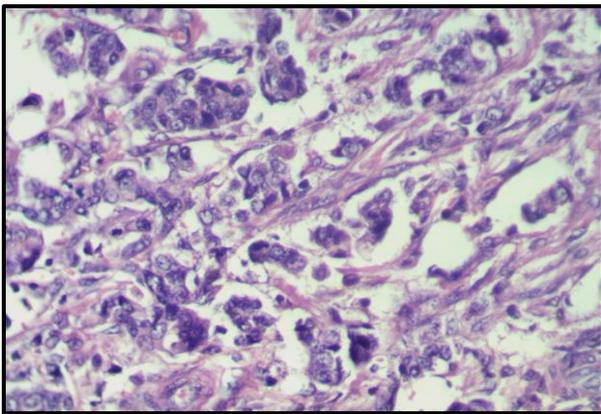
Figure 6: Histological patterns.

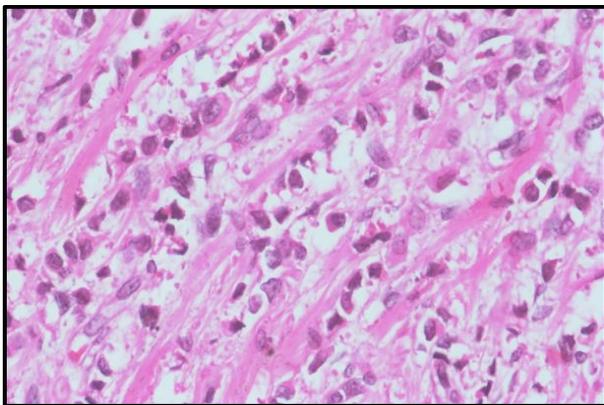**Figure 7: H and E, 400X: IDC-NST.**

Figure 8: H and E, 400X: Lobular carcinoma.
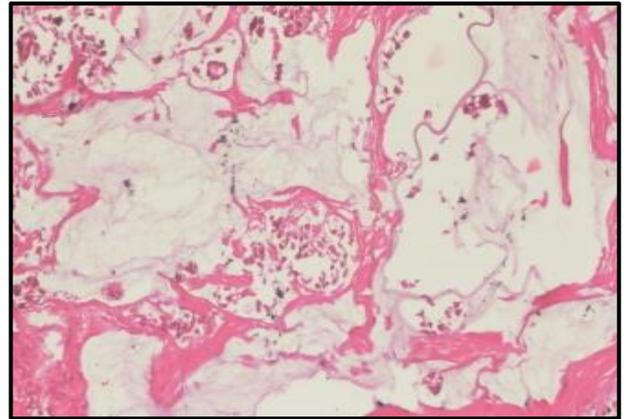

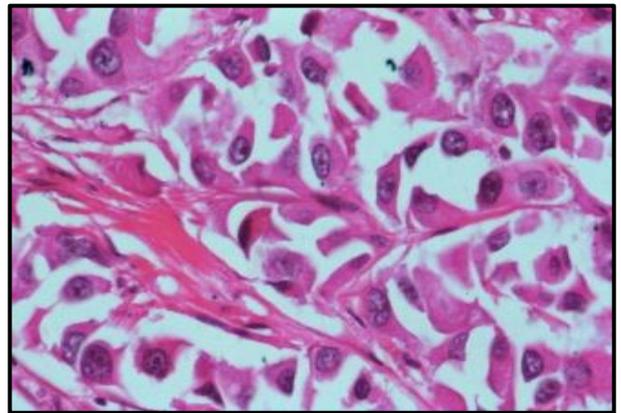**Figure 9: H and E, 400X: Mucinous carcinoma.**

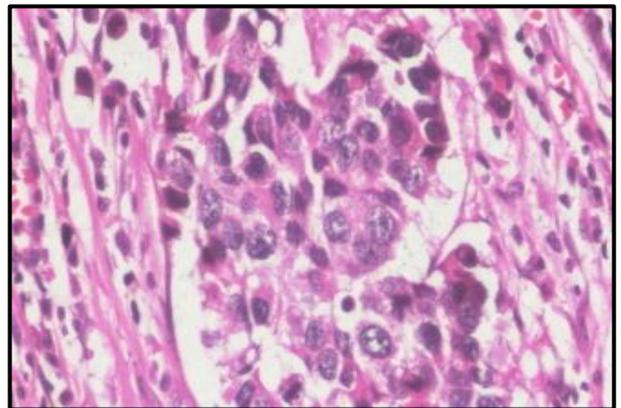**Figure 10: H and E, 400X: IDC with apocrine.**

Figure 11: H and E, 400X: Medullary carcinoma.

Out of 65 cases, 39 (60%) were ER/PR positive, 17 (26%) were triple negative, 6 (9%) cases were HER2/neu positive and 3 (5%) cases were HER2 equivocal (Figure 5). The commonest histological pattern noted was invasive breast carcinoma of no special type (90%), followed by 2 cases of lobular carcinoma and mixed type carcinoma, 1 case each of Paget's disease of nipple, medullary and mucinous carcinoma (Figure 6). The mixed types were invasive breast carcinoma, no special type (IDC-NST) with apocrine and IDC-NST with medullary. The Figures of different types of breast carcinoma are shown in Figures 7-12 and the immunohistochemistry for ER, PR and HER2 are shown in Figures 13-15.

It was seen that ER/PR positivity was more common in age groups 41-50 and 51-60 years while triple negative cases, were more common in the age group 41-50 years (Table 1). In this study, all the 13 grade 1 tumours were ER/PR positive and HER2/neu negative; thus an inverse relationship was found between HER2/neu and ER/PR receptors. Also 70% of the triple negative tumours were grade 3; which have an aggressive behaviour compared to other subtypes and were common in premenopausal women (Table 2).
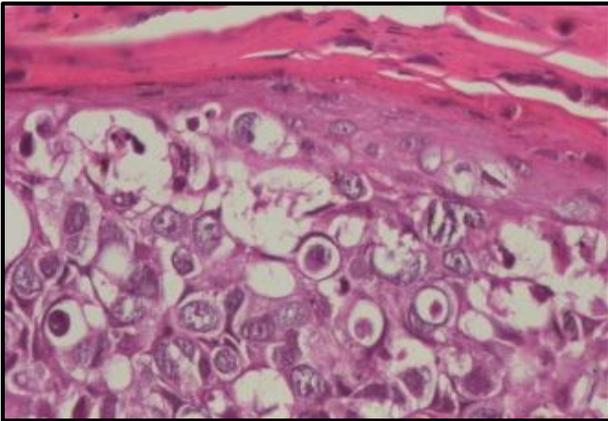
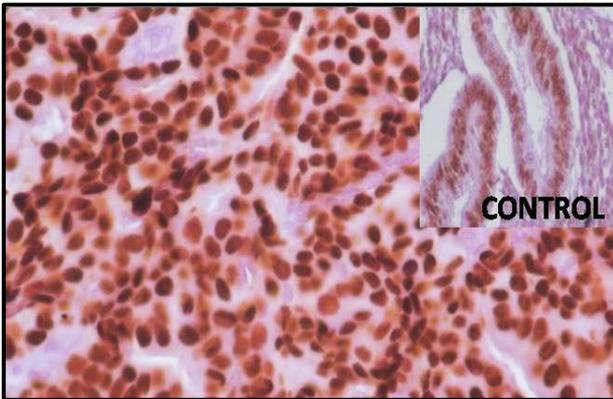**Figure 12: H and E, 400X: Paget's disease of nipple.**

Figure 13: Immunochemistry photograph showing nuclear stain positivity for ER with inset showing internal control in 400X magnification.
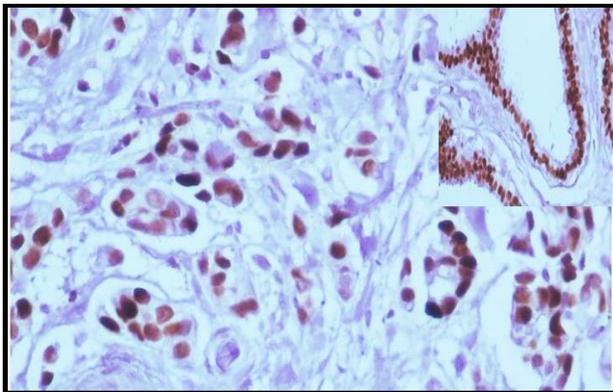

Figure 14: Immunochemistry photograph showing nuclear stain positivity for PR with inset showing internal control in 400X magnification.

DISCUSSION

The present study comprised of 65 cases of primary breast carcinoma. Majority of cases presented between 4th to 6th decades and mostly were perimenopausal women. In a study by Nidal M Almsari et al, the mean age was 47.5 years with 57% patients below the age of 50 years.[6] Literature search reveals breast carcinomas are more common in the left breast than right.[2,4,7] However, side of

breast involved has no clinical significance. In this study, right breast was marginally more affected than the left breast and a single case of bilateral breast carcinoma was noted. In this study, majority of breast carcinoma were grade 2 (46%) followed by grade 3 (34%) and grade 1 (20%) which were in concordance with the studies done by Azizun-Nisa et al and Ambroise et al; and were in discordance with a study done by Ghosh et al, which had more of grade 3 tumours (75.4%).[2,8,9]
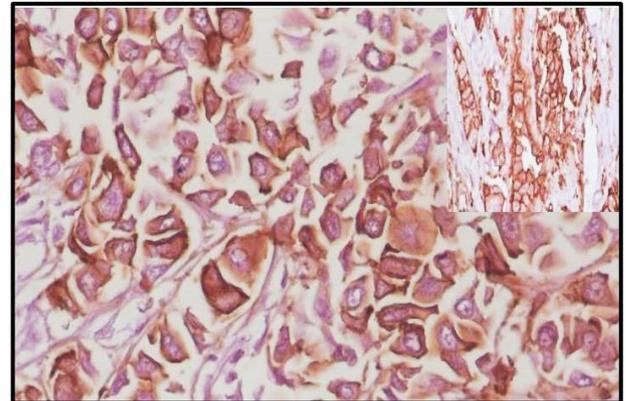

Figure 15: Immunochemistry photograph showing cytoplasmic membrane positivity for HER2 with inset showing internal control in 400X magnification.

Immunohistochemistry revealed 60% ER/PR positive, 9% HER2/neu positive, 26% Triple negative and 5% HER2/neu equivocal tumours. These results were in concordance with the studies done by Adedayo et al and Sharif et al and were in discordance with a study done by Suvarchala et al, which had higher triple negative tumours (42.19%).[4,10,11]

Literature reveals ER positivity increases with age, that is elderly patients express more ER; this was seen in this study as well.[2,8] PR positivity does not show any correlation with age.[2,8]

In the present study good correlation was found between ER/PR hormone receptor status and grade of tumour. 100% of grade 1 tumours were ER/PR positive and HER2/neu negative and 70% of grade 3 tumours were triple negative. This was in concordance with studies done by Azizun-Nisa et al and Geethamala K et al.[2,12]

In this study, no significant correlation was seen between HER2/neu and tumour grade which was similar to the studies done by Azizun-Nisa et al and Geethamala K et al and were in discordance with a study done by Ambroise et al, which had grade 3 tumours which were HER2 positive 29.9%).[2,8,12]

The limitation of the present study was the absence of correlation with Fluorescent insitu Hybridization (FISH) studies in Her2/neu equivocal cases. This test could not be done due to financial constraints.

Table 1: Association of IHC hormone receptor status with age of the patients.

Age group	ER+/PR+	ER+/PR-	ER-/PR+	HER2 +	Triple positive	Triple negative	HER2 equivocal
21-30	-	-	-	-	-	01	-
31-40	04	-	-	-	03	03	01
41-50	06	02	-	03	03	07	01
51-60	07	01	01	02	02	04	01
61-70	03	-	01	01	02	02	-
71-80	01	-	-	-	-	-	-
81-90	02	01	-	-	-	-	-

Table 2: association of IHC hormone receptor status with grade of tumour.

IHC hormone receptor status	Grade 1 (%) (13 cases)	Grade 2 (%) (30 cases)	Grade 3 (%) (22 cases)
ER+/PR+	11	08	04
ER+/PR-	-	01	01
ER-/PR+	01	03	-
HER2/neu +	-	05	01
Triple negative	-	05	12
Triple positive	01	06	03
Equivocal	-	02	01

CONCLUSION

All the grade 1 tumours were ER/PR positive and majority of grade 3 were triple negative which exemplifies the fact that higher the histological grade, lower is the hormone receptor expression. Assessment of hormone receptors for clinical management of breast cancer patients is strongly advocated to provide prognostic information and best therapeutic options. Histological grading highly correlates with the survival rate and the receptor status predicts the response to hormonal therapy.

ACKNOWLEDGEMENTS

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