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Clinicopathological Aspects, Morphological Features And Immunohistochemical Profile of Breast Carcinoma – A Study of 95 Cases.

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Abstract: *Breast cancer is the most common cancer and leading cause of death among women in our country. Clinical management of breast cancer relies on the clinical and pathological predictive and prognostic variables mainly tumor size, histological grade, staging, lymph node status, lymphovascular invasion and hormonal receptor status. The purpose of this study is to assess the clinical data, evaluate the morphological parameters in the breast cancer patients and their correlation with immunohistochemical analysis. 95 cases of breast carcinoma from January 2015 to December 2016 reported in the Department of Pathology, Government Royapettah Hospital, Kilpauk Medical College, Chennai were included in the study. Relevant clinical data, mode of presentation, tumor laterality, gross and microscopic features were noted. Haematoxylin and Eosin stained tissue sections slides were examined.In the present study, most commonly affected female population were in the age group 41 -59 years(69%). Majority of tumors were diagnosed as infiltrating ductal carcinoma NOS type (77%), followed by invasive lobular carcinoma (10%), mucinous carcinoma (1%) and others.Most of the tumors were histopathological grade II followed by grade III. Lymphovascular invasion was found to be 3.1%. ER (52 %), PR (22.6%), and HER2/neu (21.5%). Histopathological grade was found to be inversely proportional with receptor positivity, which showed that as the grade increases, receptor positivity will decrease both of which indicates poor prognosis. The present study shows a significant correlation between various pathological aspects, histopathological grade and immunohistochemical status of breast carcinoma which will be helpful to some extent in determining the prognosis, treatment modalities and response to therapy in practice.*

Keywords: *Breast carcinoma, histopathological grading, hormone receptor status.*

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I. Introduction

Breast cancer is the most common cancer in adult females (22%) and ranks second among cancer deaths with a high prevalence both in developed and developing countries[1,2]. About 75,000 new cases have been diagnosed every year in Indian women[3]. The incidence of breast cancer ranges from 3.9% to 101.1% per 100,000 female population[4]. Early detection and management of disease with proper interventional measures has reduced the mortality rate during the last two decades. Also identification and prevention of risk factors helps to a certain extent in reducing the mortality of disease.Prognosis and treatment of breast cancer are influenced by the classic parameters such as tumor size, histopathological grade and subtype, lymph node metastsis and hormone receptor status of the tumor.Regarding receptor status, generally the expression of ER and PR in Invasive breast carcinoma is associated with a better outcome when compared to the expression of Her2/ neu which is associated with a poor outcome. Likewise, carcinomas with high grade will have receptor negativity which is found to be an important variable in predicting the prognosis of the patients. The present study was conducted in our institution to evaluate the clinical data, relevant gross and microscopic features, histological type ,grade, lymph node status, immunohistochemical profile and to assess the prognosis of breast cancer patients.

II. Materials And Methods

The present study was undertaken from January 2015 to December 2016 in the Department of Pathology, Government Royapettah Hospital (GRH), Kilpauk Medical College, Chennai. 95 cases diagnosed as breast cancer from Modified Radical Mastectomy specimens were included in the study, of which post chemotherapy / radiotherapy patients were about 25 in numbers.Clinical details including age, mode of presentation, tumor laterality, menstrual and obstetric historywere recorded. Immunohistochemical profile for the reported breast

carcinoma cases during the year 2015 and 2016 were obtained from the Department of Oncology, GRH, KilpaukMedical College, Chennai.Formalin fixed paraffin embedded tissue blocks were used, and further stained with Hematoxylin and Eosin stain and subjected to histopathological examination.According to Nottingham modification of the Scarff Bloom and Richardson grading system, invasive breast carcinomas were histologically graded andstaging of the tumor was done by using TNM staging system.

III. Results

The present study showed that out of 95 cases of breast carcinoma , 94 cases were female patients and one patient was male. The age group of the study population ranged from 26 years to 75 years of age. Majority were in the age group of 41 -59 years of age (69%) which is shown in table-1. About laterality of the breast , left sided breast was marginally more involved (66%) than right sided breast (23%) and in only one female patient, bilateral breast carcinoma were reported. Grossly, the tumor size ranges from 1.5 cms upto 10 cms, and most of the tumors were more than 5cms in size (58.7%). Only about 2% of the tumors showed nipple areola involvement. Totally,out of 95 cases including the male patient, microscopically Infiltrating ductal carcinomas NOS type was found to be the most common histological type (77%) of breast carcinoma.Remaining cases were found to be invasive lobular carcinoma(10%), mucinous carcinoma(1%) and others (11%).Onecase with tumor size of about 10 cm were reported as Angiosarcoma(1%) in a 27 year old female patient.

Table –1. Agewise distribution of breast cancer cases in the present study

AGE (Years)	No.of cases	Percentage (%)
21-30	2	2.1
31-40	11	11.5
41-50	29	30.6
51-60	37 (male-1)	39
61-70	14	16.8
Total	95	

Infiltrating ductal carcinomas (IDC) with cribriform pattern was seen in 7 cases, IDC with comedonecrosis was seen in 5 cases, IDC with associated Ductal Carcinoma in situ component (DCIS) was seen in 5 cases and IDC with metaplastic change or bone formation was found in one case. Lymph node metastasis was observed in about 46 cases(48.4%)of which 2 cases showed maximum number (18/18)of lymph nodes involved by the tumor. Lymphovascular invasion was observed in (3.1%) Of the 25 post chemotherapy/ radiotherapy patients, residual tumor in the breast was found to be in 8 caseswith lymph node metastasis in 3 cases and 17 cases showed the absence of residual tumor in the primary site with lymph node metastasis in about 6 cases. The microscopic features of the above 17 cases revealed only changes of hyalinization,lobular atrophy, inflammatory response and fibrosis in the breast. On analysis including the split up of post chemotherapy/ radiotherapy cases per grade, it was observed that most of the tumors were under Grade II- 46 cases (48.4%), followed by Grade III(22.1%) and Grade I(18%) which includes 21 and 17 cases respectively as shown in table-2.7/17 cases of grade I tumors, showed cribriform pattern which indicates that these tumors were of low nuclear grade and have better prognosis. Also,7 cases of left sided breast carcinoma with right axillary node metastasis and 5 cases of right sided breast with left axillary node metastasis were observed in this study.

Table -2. Histopathological grading of invasive breast carcinoma

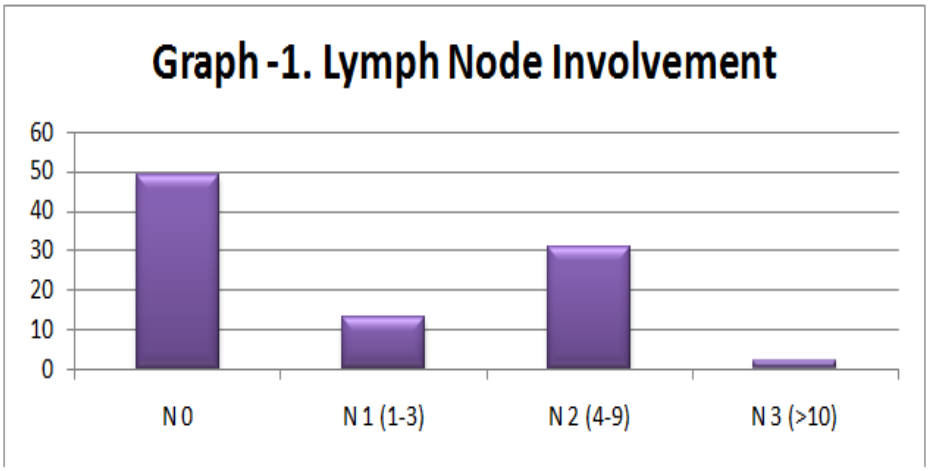
TUMOR GRADE	NO.OF CASES	PERCENTAGE(%)
Grade I	17	17.8
Grade II	46	48.4
Grade III	21	22.1
Nil tumor residue	11	11.5
Total	95	

Using TNM staging, majority of the tumors were under stage $T_3N_2M_0$(46.3%)followed by $T_2N_1M_0$,$T_1N_0M_0$ and $T_4N_3M_0$which is shown in table -3 and graph-1. On observation, this study showed that majority of cases were of T_3 stage (> 5cms) and N_2 stage involving about 4 -9 lymph nodes. 2 cases with tumor size of about 10cms have been put up under the category of locally advanced breast cancer. Immunohistochemical status was available for 84 cases and showed that,of grade I and grade II tumors,ER was found to be positive in 44 cases and PR was found to be positive in 19 cases.None of the cases showed Her2 /neu expression in grade I and II tumors. One case of Grade II and 17 cases of Grade III tumors showed HER2/Neu positivity. Also majority of the grade III tumors were ER and PR negative. Triple negativity was

seen in 3 cases of grade III tumors, in which the data was shown in table -4 & table- 5. On analysis, this study showed that higher the grade , lower the expression of receptor indicating poor prognosis to the patients. It also revealed a significant correlation betweenthe grade of the tumor and immunohistochemical status.

Table-3. Pathological staging of invasive breast carcinoma

STAGE	NO OF CASES	PERCENTAGE
1	12	12.6
2	26	27.5
3	44	46.3
4	2	2.1
Nil tumor residue	11	11.5
Total	95	



No.of cases No.of lymph nodes involved in each stage

Table-4. Immunohistochemical status of 84 cases of breast carcinoma

HORMONE RECEPTOR	NO OF CASES	PERCENTAGE
ER	44	52.3
PR	19	22.6
HER2/Neu	18	21.5
Triple negative	3	3.6
Triple positive	0	0
Total	84	

Table-5. Correlation of tumor grade with hormone receptor status

HORMONE RECEPTOR STATUS	GRADE I %	GRADE II %	GRADE III %
ER	11 (64.7%)	33 (70.2%)	0
PR	6 (35.3%)	13(27.7%)	0
HER2/Neu	0	1(2.1%)	17 (85%)
Triple negative	0	0	3 (15%)
Triple positive	0	0	0
Total	17 (100%)	47(100%)	20 (100%)

IV. Discussion

Breast cancer is the most common cancer among women in India as well as western countries. The reliable prognostic factors include age, tumor size , histological type, tumor grade , stage and hormonal receptor status.According to Madras Metropolitan Tumor Registry statistics, Chennai, the breast cancer had higher incidence rate of about 54.6% to 104.1% per 100,000 population and the susceptible age group was 40 – 59 years female[5].The present study shows that 69% of the female population were in the age group 41 -59 years old which is similar to that reported in Indian Literature.Also, Acharya et al in his study observed the most frequent age group with breast cancer was 41 -55 years old[6]. Similarly, thestudies done by Ambroise et al [7], Rhodes et al[8] and Suvarchala et al [9] showed the age range between 51- 60 years. As per World Health Organization (WHO) literature, the occurrence of breast cancer were more frequent in the left breast with a reported left to right ratio was 1.07 to 1[10.] In the present study too, left breast was marginally involved when compared to the right and a single case of bilateral breast carcinoma was also noted. In many studies done by

Rosen et al[11], Ellis et al[12], Raina et al[13], Page and Anderson[14],Infiltrating ductal carcinoma NOS type turned out to be the most common type of breast carcinoma followed by lobular carcinoma and other types. The distribution of histopathological types in this study is almost similar to the above studies. The present study showed that majority of the tumors were grade II,which is in concordance with other well known studies which is shown in the table -6.

Table-6. Comparison of grade of the tumor of the present study with other studies

STUDY	GRADE I	GRADE II	GRADE III
Adedayo et al 2009(15)	21.2	38.4	35.9
Ambroise et al 2011	9.4	57.3	33.3
Suvarchala et al 2011	28.12	42.18	29.69
Azizun-Nisa et al 2008(16)	6.7	55.3	38
Present study 2017	17.8	48.4	22.1

Immunohistochemical status showed that 52.3% ER positive, 22.6% PR positive, and 21.5% Her2/Neu positive, which were in concordance with other studies done by Ghosh et al[17], Sharif et al[18]and Ambroise et al[7] and depicted in the table - 7. We established a significant correlation in the present study between grade of the tumor and hormonal receptor profile. Like this study, a similar correlation was obtained in other Indian and western studies[6,8,15] which is shown in table -8..

Table -7. Comparison of hormone receptor status of the present study with other studies

STUDY	ER AND PR (%)	HER2/NEU (%)
Sharif et al 2010	62.8	28.1
Ambroise et al 2011	47	27
Ghosh et al 2011	51.2	24.8
Present study 2017	52.3	21.5

Table- 8. Comparision of tumor grade and hormone receptor status of the present study with other studies.

STUDY	TUMOR GRADE	HORMONE RECEPTOR STATUS
Azizun- Nisa et al 2008	Grade 1 No correlation	70% ER+/PR+ Her2/neu
Ambroise et al 2011	Grade 1& 2 Grade 3	47% ER+, 27%Her2/neu,25%Triple negatives
Suvarchala et al 2011	Grade 2	51.85% ER+/PR+
Present study 2017	Grade 1 & 2 Grade 3	52.3% ER+,22.6% PR+ 21.5% Her2/neu & 3.7% triple negatives

V. Conclusion

The present study reveals that infiltraring ductal carcinoma NOS type was the predominant histological type of breast cancer, with majority of grade 1 and 2 tumors were ER positive and some of the grade 3 tumors were Her2 /neu positive.Triple negative tumors were observed in some of the grade 3 tumors which intensifies the fact that higher the tumor grade, lower is the hormone receptor expression. This study highlights the significant correlation between the grade of the tumor and the hormone receptor profile which provides an important information in assessing the prognosis and predicting the patients response to hormone therapy.

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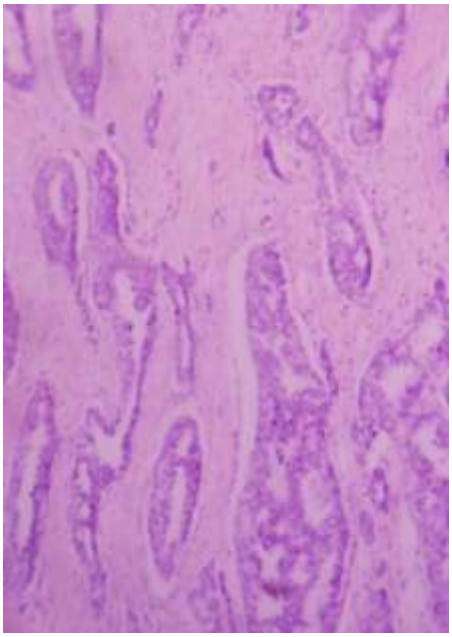

Fig-1. IDC Grade I, H&E stain 100X

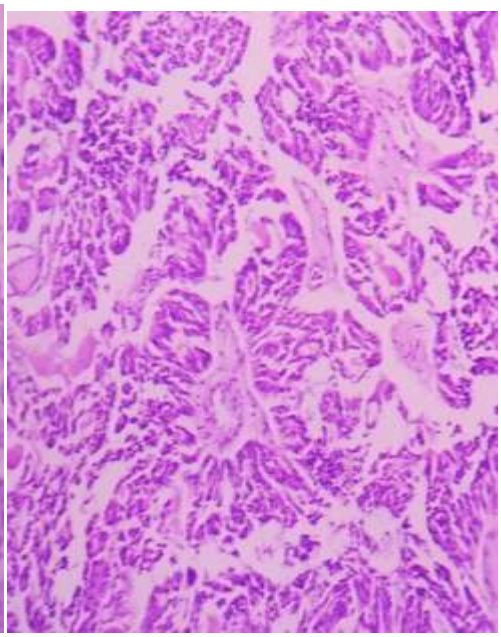

Fig-2. IDC Grade II, H&E stain 100x

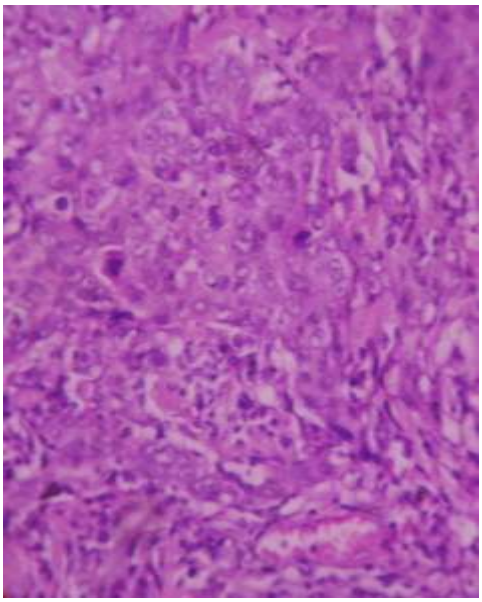

Fig-3. IDC Grade III, H&E stain 400x

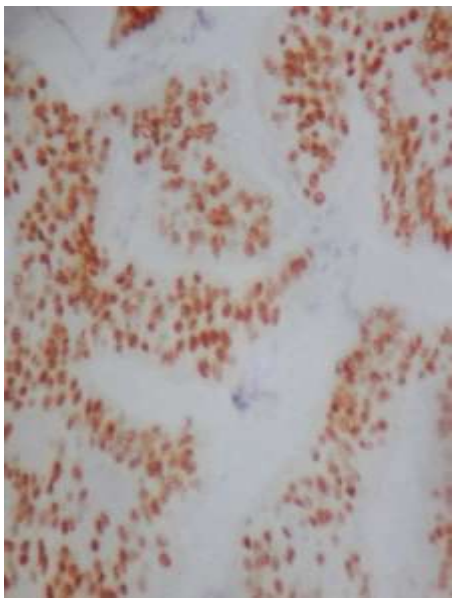

Fig-4. IHC- ER Stained cells 100x

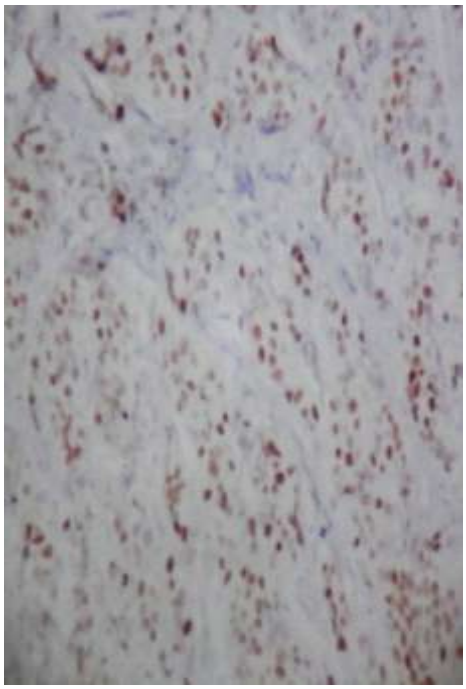

Fig- 5. IHC- PR Stained cells 100x

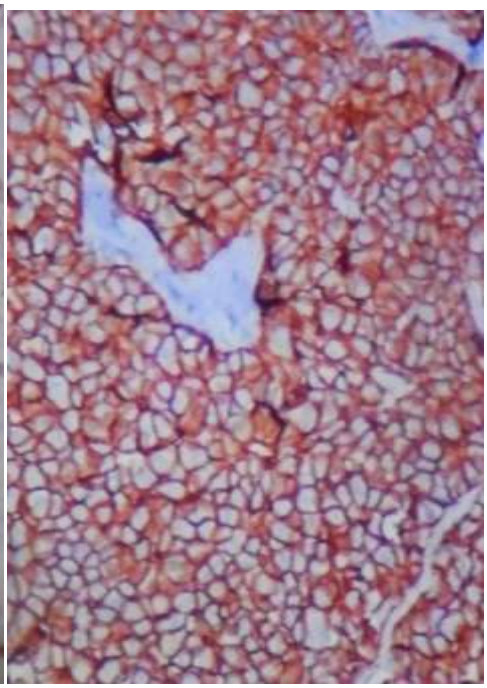

Fig – 6. IHC- Her2/ Neu stained cells 400x

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