

# Comprehensive Histopathological Examination and Breast Cancer: An Institutional Analysis

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## ABSTRACT

**Background:** The histological patterns and other microscopic parameters play important role in the therapeutic management and assessment of the prognosis of the carcinoma breast. As this carcinoma shows heterogeneity, a careful gross examination followed by a more detailed examination of tissue sections is the backbone of the histopathological analysis.

**Methods:** Total of 103 cases of breast carcinoma were included in the study. Histopathological reports along with detailed gross examination findings were re-assessed for various histological patterns and associated features. Data obtained was analysed.

**Result:** Gross examination findings showed 9.4% multicentricity of the tumor. Histopathology revealed infiltrating ductal cell carcinoma not otherwise specified (IDC NOS) as most common histologic type (77.6%), I as common grade (45.8%) and IIA as common stage (28%) with other unique microscopic characteristics.

**Conclusion:** Gross findings were more or less similar with results shown in the literatures except 9.4% multiple invasive pattern of the tumor. Different histopathological findings were papillary carcinoma as second common histological pattern, histologic grade I as common grade, evidence of lymphovascular invasion less common than perineural invasion. In addition atypical ductal hyperplasia was seen associated with papillary carcinoma commonly and desmoplasia with N0 tumor.

**Keywords:** Carcinoma Breast, Gross Examination, Extranodal Extension, Lymphovascular Invasion

## Introduction

Pathologist is a hidden consultant in the management of carcinoma breast. The standardization in cancer reporting improves the competence and quality of the reporting. Breast carcinoma exhibits a wide scope of histopathological features, different subtypes that have specific clinical outcome.<sup>[1]</sup> The careful grossing and optimal light microscopy helps in providing information about the prognosis, parameters for therapeutic management and platform for research in carcinoma breast.<sup>[2]</sup> The present analysis was done to assess the various histological patterns and associated microscopic parameters of carcinoma breast patients.

## Materials and Methods

Total of 103 carcinoma breast specimens were received in the department of pathology including 18 postneoadjuvant chemotherapy patients. The cases were studied retrospectively and data obtained by gross examination and histopathology was re-analysed.

All the specimens were weighed, fixed in the 10% neutral buffered formalin for minimum 8 to 12 hours. The base of modified radical mastectomy (MRM) specimens was painted before cutting and grossing. Specimens of breast conservative surgeries were painted for base as well

resection margins (Fig 1). The tumor centricity and size was noticed with involvement of skin, nipple and areola complex (NAC). Distances of surgical cut margins were measured along with base of tumor. Representative sections were submitted along with minimum of four pieces taken from tumor including adjoining grossly unremarkable area and one random piece from adjacent breast tissue at the distance of 5cms if possible. Maximum number of lymph nodes (LNs) was dissected out. H&E stained sections were examined under light microscope and tumors identified were categorized as per WHO classification. Immunohistochemistry was performed for estrogen receptors (ER), progesterone receptors (PR) and Her2neu. Allred scoring system was applied for the Interpretation of ER and PR tumor biomarkers. Her 2neu status was reported as per revised reporting guidelines of the American Society of Clinical Oncology (ASCO)/ College of American Pathologists (CAP). A proforma, broadly based on RCPATH and CAP datasets was used for reporting of carcinoma breast.<sup>[3]</sup> All the recommended parameters were noted. Some additional parameters such as desmoplasia, atypical ductal cell hyperplasia, fibrocystic disease and tumor infiltrating lymphocytes (TILs) were also analysed and mentioned in the microscopic description. The evaluation of TILs was done as recommended by an

International TILs Working Group 2014. Furthermore the stromal TILs were categorized as group (G)1 (0-5%), G 2 (>5-20%), G 3 (>20-70%) and G 4 (>70%).<sup>[4]</sup> While reporting breast conservative specimens, margins of 5 mm and more were considered as clear, 1-5 mm as close and less than 1 mm as involved margin microscopically.<sup>[5]</sup>

## Result

On gross inspection of breast carcinoma specimens without preoperative neoadjuvant chemotherapy exposure, tumor size varied widely with majority of the cases showing single growth only. Modified bloom Richardson score, histologic grading and pTNM staging were done along with revealing of other parameters (Table 1).

The assessment of the immunohistochemical marker ER, PR, and Her2neu was done in 59 cases. Triple negative (ER, PR, and Her2Neu negative) were found to be the

commonest group comprising 45.6% of all the cases followed by ER and PR both positive 20.3%, ER positive 10.0%, PR positive 8.4%, Her2neu 8.4% and triple positive (ER, PR, and Her2neu positive 8.4%) (Fig 2). In postchemotherapy cases size of the tumor varied from 7.8x7x2.8cms to 3.2x2.5x1.8cms with no multicentricity. Involvement of nipple areola complex was seen in 11.1% cases without any skin involvement. More than 10 LNs were dissected out in 82.3% where as rest of the cases showed less than 10 lymphnodes. Microscopically tumor cells were seen in 88.4% with 47% lymph node metastasis. No tumor cells were seen in rest of the 11.6% of the cases but lymph node metastasis noticed in 50%.

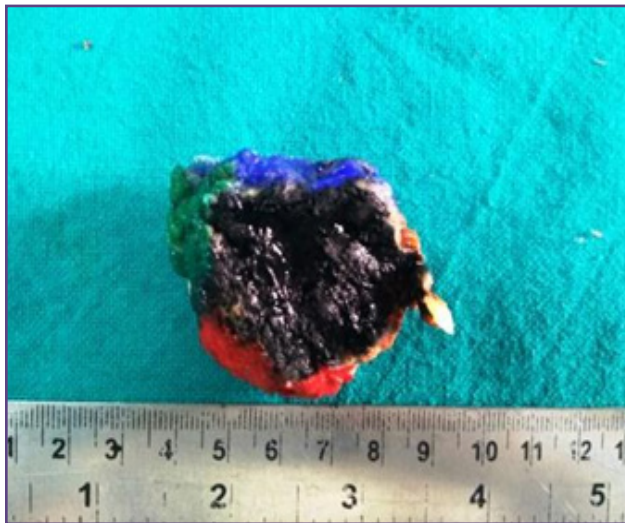
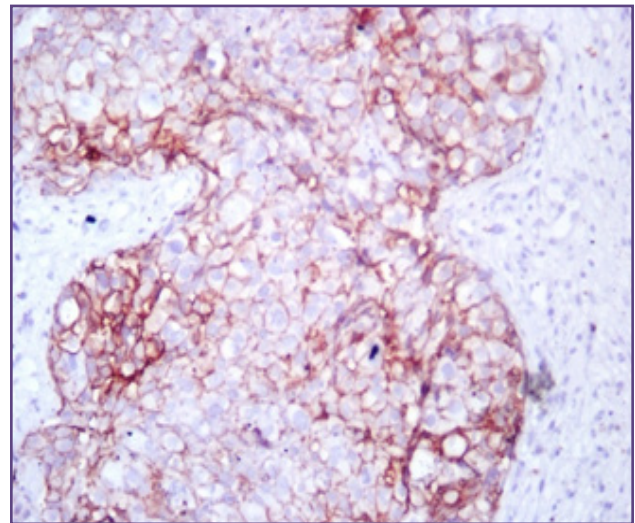
Fibrocystic disease was seen in adjacent breast tissue in total of 7.7% of the cases of carcinoma breast irrespective of previous treatment. Stromal TILs (G4) showed association with high grade and high stage of carcinoma.

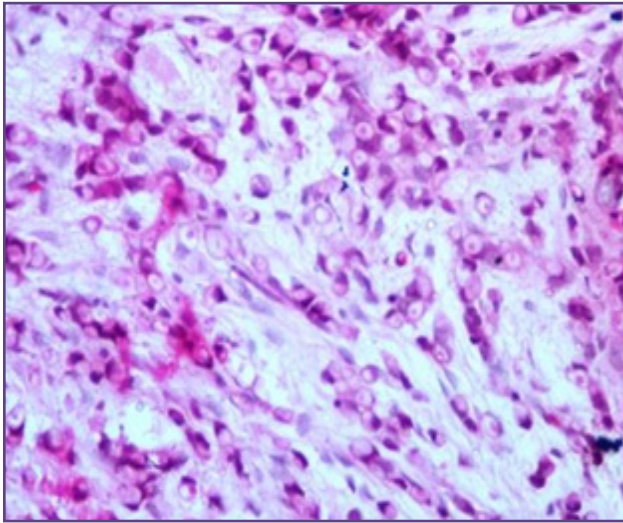
**Table 1: Various histopathological parameters and findings.**

Sr.no	Parameters	Observations
1.	Size	5.6x2.6x1.5cms ( $\pm$ 3.8x1.4x1.5cms) Mean ( $\pm$ SD)
2.	Multicentric tumor	9.4%
3.	NAC involvement	16.4%
4.	Skin involvement	9.0%
5.	Lymphnodes dissected out	>10 (96.1%), <10 (3.8%)
6.	Microscopic type	IDC NOS (77.6%)
7.	Histologic grade	I (45.8%) II (42.3%) III (11.7%)
8.	pTNM stage	I (18.8%) II (53.8%) III (26.9%)
9.	Extranodal extension (ENE)	3.5%
10.	Margin status (positive)	27.7%
11.	Perineural invasion (PNI)	7.0% (33.3% seen in cases without LN metastasis)
12.	Lymphovascular invasion (LVI)	5.8%
12.	Desmoplasia	11.7% (70% seen in cases without LN metastasis)
13.	Atypical ductal hyperplasia (ADH)	3.5%
14.	Tumor infiltrating lymphocytes (TILs)	G1 (4.6%) G2 (77.8%) G3 (14.3%) G4 (3.3%)

**Table 2: Comparison of histopathologic patterns of carcinoma breast.**

Author/ Authors, year	Types of carcinoma				
Saxena et al, 2005 <sup>[16]</sup>	IDC NOS (88.2%)	ILC (3.7%)	(Mucinous carcinoma 1.1%)	DCIS (1.1%)	Other types (5.9%)
Kakarala M et al, 2010 <sup>[17]</sup>	IDC NOS (69.1%)	ILC (4.2%)	Invasive mixed carcinoma (4.2%)	Inflammatory carcinoma (1.4%)	Other types (21.1%)
Sandhu et al, 2010 <sup>[18]</sup>	IDC NOS (96.9%)	Mucinous carcinoma (1.4%)	Medullary carcinoma (1.0%)	Paget's disease (0.3%)	Other types (0.4%)
Mohapatra M et al, 2013 <sup>[19]</sup>	IDC NOS (95.5%)	ILC (1.7%)	Mucinous carcinoma (1.1%)	Papillary carcinoma (1.1%)	Other types (0.6%)
Nigam et al, 2014 <sup>[20]</sup>	IDC NOS (81.4%)	Medullary carcinoma (10.36%)	Mucinous carcinoma (2.74%)	ILC (2.44%)	Other types (3.0%)
Takalkar UV et al, 2016 <sup>[21]</sup>	IDC NOS (99.2%)	Medullary carcinoma (0.3%)	Paget's disease (0.3%)	-	Other types (0.2%)
Singh SK et al, 2016 <sup>[22]</sup>	Scirrhus carcinoma (78.94%)	Medullary carcinoma (10.53%)	Mucinous carcinoma (4%)	Papillary carcinoma (4%)	Other types (2.5%)
Gangadaran SGD, 2016 <sup>[23]</sup>	IDC NOS (94%)	Lobular carcinoma (3%)	Metaplastic carcinoma (0.01%)	Medullary carcinoma (0.01%)	Other types (2.9%)
Heda K et al, 2017 <sup>[24]</sup>	IDC NOS (83.8%)	Lobular carcinoma (11.1%)	Mucinous carcinoma (2%)	Comedo carcinoma (1%)	Other types (2.6%)
Current results	IDC NOS (77.6%)	Papillary carcinoma (4.7%)	Medullary carcinoma (3.5%)	Mucinous carcinoma (2.3%)	Other types (11.9%)

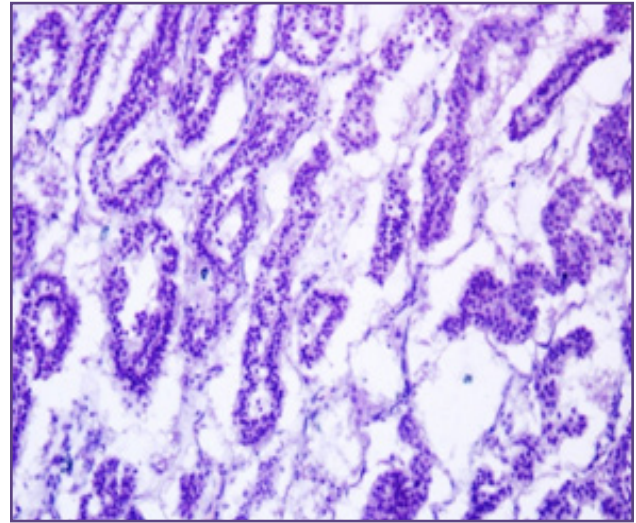
**Fig. 1: Specimen of breast conservative surgery.****Fig. 2: Her2Neu positive (IHC section 40X).**



**Fig. 3: infiltrating lobular carcinoma (H&E stained sections 40x).**

### Discussion

Pathologists deal primarily with structure. In addition to providing diagnosis, standardized report provides information to be used to aid in selecting primary or adjuvant therapy, estimating prognosis as well as data for research. Role of detailed gross examination is crucial in attaining the accurate histopathology findings. A careful gross examination was done as it is important to define the stage of tumour for post operative adjuvant treatment.<sup>[6]</sup> The multiple invasive tumor was noticed in 9.4% of the cases, more commonly associated with infiltrating lobular carcinoma (ILC) (33%). In the previous studies done the incidence of multicentric foci in the breast has been reported to vary from 18 % to 69% with submission of 1–2 random samples from each quadrant to 5 mm sections of whole breast respectively.<sup>[7,8]</sup> Multiple invasive tumor upgrades the stage of the carcinoma and can show different differentiation hence challenges the management.<sup>[9,10]</sup> NAC involvement was seen in 16.4% and amongst that 18.1% involvement was seen microscopically. Whereas in a study done by Wang J et al, 9.5% NAC involvement was seen with only 28% gross involvement.<sup>[11]</sup> In post chemotherapy cases 11.1% NAC involvement was seen. The number of atleast 10 axillary lymphnodes is generally considered an adequate axillary lymphnodes dissection for reliable LN status. At our institution >10 LNs were dissected out grossly in 96.1% with median number of LN removal of 15. On the otherhand <10 LNs were dissected out in 3.8% cases only and the factor was of matted lymph nodes in 33% of the cases resulting in inadequate separation LNs.<sup>[12]</sup> In cases of post chemotherapy more than 10 LNs were dissected out in only 82.3%.



**Fig. 4: Micropapillary carcinoma (H&E stained sections 40x).**

On histopathological examination, IDC NOS was commonest (77.6%) amongst all microscopic types of carcinoma breast followed by papillary carcinoma (4.7%), ILC (3.5%) (Fig 3), medullary carcinoma (3.5%) (Figure 4), micropapillary carcinoma (2.3%) (Fig 4), mucinous carcinoma (2.3%), apocrine type (1.1%), oncocytic type (1.1%), neuroendocrine type (1.1%), metaplastic (1.1%) and mixed type (1.1%). National Cancer Registry Program has shown that, IDC NOS is commonest breast cancer followed by lobular carcinoma in the hospital-based cancer registries in Mumbai, Bangalore, and Thiruvananthapuram during 1984-1993.<sup>[13]</sup> In a study done by Nigam et al, IDC NOS was the commonest microscopic type (81.40%) followed by medullary carcinoma (10.36%) and mucinous carcinoma (2.74%). Tumor grading was done in all the cases as per Modified-Bloom Richardson method of grading and most common grade found was grade I (45.8%) followed by grade II (42.3%) and Grade III (11.7%). Triple negative (45.6%) was the commonest finding upon immunohistochemistry examination.<sup>[14]</sup> As seen in a work done by Pradhan et al most common tumor grade was II (38.7%), followed by I (35.4%) and III (25.8%).<sup>[15]</sup> Pathological TNM stage IIA (28%) and IIB (25.8%) were seen more commonly followed by stage IA (18.8%) and stage IIIB (12.9%), IIIC (7%), IIIA (7%) in the present study. Whereas studies done by Nigam et al, Wani et al and Saxena et al showed IIIA, IIB and IIIB as most common stage at presentation in carcinoma breast patients (Table 2).<sup>[14,16,17]</sup>

Detailed pathological examination of the tumour also provides parameters for prognosis and research. It is

important to mention centricity of the tumour in the report, as evidence of satellite nodule in addition to up gradation of the stage, as per recent studies also can show different differentiation. As seen in the current study, 1% of the cases with multicentre lesions have shown more than one differentiations of squamous cell carcinoma, micro papillary carcinoma along with infiltrating ductal cell carcinoma. Still the prognostic impact of multiple lesions has been poorly studied and potentially unfavourable effect of multifocality is a subject to investigation.<sup>[17]</sup> The size and number of metastatic lymphnodes along with evidence of EN extension was mentioned in each report. ENE should be included in the reporting format to check the extent of metastasis. In our case ENE was seen in 3.5% and 60%, 40% of its association was noticed with TNM stage IIIA and IIIC respectively irrespective of low to intermediate grade of the tumor. In post chemotherapy case, no ENE was noticed.<sup>[18]</sup> In situ component is one of the important prognostic parameters. It was especially mentioned (3.8%) where detected. Amongst that 66.6% cases were associated with stage I and grade I tumors. In one case there was presence of an extensive intraductal component with foci of invasion which can be associated with recurrence of carcinoma.<sup>[19]</sup> ADH was seen associated with carcinoma in 3.5% of the cases, with more common association noticed with papillary carcinoma. Whereas fibrocystic disease was detected in 7.7% of the total cases irrespective of chemotherapy exposure.<sup>[20,21]</sup> Desmoplasia was seen in 11.7% of the cases and two third of the cases were seen in N0 stage of carcinoma.<sup>[22]</sup> LV invasion is an important independent prognostic factor, especially in patient with T1 node negative breast cancer. In our case 5.8% LVI was detected and amongst that 20% was detected in T1 N0 cases.<sup>[23]</sup> PNI is a comparatively rare histopathological feature in invasive breast carcinoma occurring 10 times less frequently than LVI.<sup>[24]</sup> But in our experience perineural invasion was detected in 7.0% of total cases with 33.3% association without LN metastasis. The status of surgical margins was especially mentioned in all the BCS specimens, 27.7% cases showed positive margin status. This is important for the oncologists as well as surgeons to estimate any chance of local recurrence and to decide mode of adjuvant therapy.<sup>[25]</sup>

TILs are considered as important prognostic factors for the carcinoma and their morphological estimation has attained drive. In the current analysis, increased number of stromal TILs was noticed in increased grade and stage of the tumor.<sup>[26]</sup>

## Conclusion

A comprehensive pathology report is good parameters for clinicians in deciding the treatment plan and prognosis.

Tumor diversity and heterogeneity may be the reason for variation in histological patterns and parameters of carcinoma.

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