

## Histopathological Study of Malignant Neoplastic Lesions of Breast

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### Abstract

Breast cancer is a leading cause of mortality and morbidity among women worldwide. The high mortality associated with breast cancer is linked to the aggressiveness of the tumor which depends to a large extent on the histopathological subtypes. It is a heterogeneous disease, comprising multiple entities associated with distinctive histological and biological features, clinical presentations and behaviours and responses to therapy. Histological grade has been incorporated in multiple, validated, prognostic algorithms to determine breast cancer therapy, such as the Nottingham Prognostic Index. Many studies have tried to identify prognostic factors for breast cancer with nodal status and histopathologic subtypes featuring prominently as prognostic indices. This study was a retrospective analysis of all consecutive breast cancer specimens study from January 2011 to September 2016 biopsysubmitted to the Pathology Department of Hassan Institutional Medical Sciences, Hassan. Prominent histomorphological features, grading, typing, Lymphovascular invasion, lymph node involvement and involvement of the surgical margins were studied in detail. The aim of this study was to know the age incidence patterns for different histopathologic types of carcinoma and to know the involvement of deep resected margin and number of lymph nodes by malignant cells.

**Keywords:** Breast Cancer; Histopathology Grading; Resected Margin; Nottingham Prognostic Index.

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### Introduction

The breast is a modified sweat gland composed of both epithelial and connective tissue elements. Therefore, neoplasms arising from these elements have to be classified separately. The present study is based on the classification proposed by WHO in 2003 [1]. Breast carcinomas among women are extremely diverse in clinical and histopathologic features, suggesting that these tumors also vary in etiology [2].

Breast cancer is the commonest cancer in urban Indian women and the second commonest cancer in the rural women next to cervical carcinoma. Due to general indifference towards the health of females in the Indian society, lack of an organized breast cancer screening program, and paucity of diagnostic aids, majority of breast cancers are diagnosed at a relatively advanced stage [3]. The standard prognostic factors,

recognized by the National Cancer Institute in 1990, include lymph node status, tumor size, nuclear grade, steroid receptor content, tumor type, and cellular proliferation rate [4]. Histological grade forms part of the multifactorial Nottingham prognostic index, together with tumour size and lymph node stage and used to stratify individual patients for appropriate therapy [5]. Some recent studies have indicated that reproductive factors, as well as other hormone-related risk factors, affect the risk of histological types of breast cancer differently possibly reflecting a different etiology of disease according to histological type [6].

### Materials & Methods

This was a retrospective, register-based analysis of all consecutive breast cancer specimen submitted to the pathology department of Hassan Institutional Medical Sciences, Hassan from January 2011 to September 2016. All records and clinicopathological information of patients with the diagnosis of breast cancer were retrieved from the pathology registers and request forms. Information such as age, sex and

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(Received on 04.07.2017, Accepted on 22.07.2017)

laterality were retrieved from the request forms under the study period January 2011 to September 2016. Cases with incomplete data entries were invalidated. Tissue were fixed in 10% formalin and processed to make multiple paraffin blocks. The sections were cut at 5 micron thickness and were stained with hematoxylin and eosin. For malignant neoplasms sections included tissue from the neoplasm site, nipple and areola, deep surgical margin, nearest peripheral surgical margin to the tumor, adjacent breast and lymph nodes if present. In cases of missing or broken archival slides fresh sections were cut from blocks and stained with Haematoxylin and Eosin and analysed again. Breast cancers were typed using the recent histopathological typing of breast tumour. The gross pathology of the specimens and the histopathological findings were recorded in detail. The breast neoplasms were classified according to the histological classification of breast neoplasms given in the WHO Classification of Neoplasms, 2003. The data were analysed for simple means and percentages.

## Results

A total of 98 cases of malignant breast tumours were recorded during the January 2011 to September 2016 study review. The specimens were received most commonly as modified radical mastectomy. Out of the 98 cases of breast cancers analysed, all were in females. The age range of female patients included in the study was between 28 years and 85 years with a mean age of 56.5 years. Majority of the cases were in age range of 40 - 70 years [74.2%] followed by the fourth decade [17.4%]. Invasive ductal carcinoma (no special type) constituting the majority of breast cancers (83.67%) while malignant phylloides was the least common representing 1.02%. Invasive lobular carcinoma ranked second (5.1%), Under the special types of malignant breast carcinoma, medullary carcinoma ranked first with 6 cases recorded in our series, followed closely by 2 cases of mucinous carcinoma and 1 cases, each of papillary and signetring cell carcinoma. No cases of ductal and lobular carcinoma in situ were recorded. Breast carcinomas were observed to occur more on the right breast than the left breast with the right breast accounting for 62.4% and the left 37.6%. No case recorded to occur bilaterally. 15 cases (15.30%) show involvement of nearest resected margin by tumor cells. Lymphovascular invasion was noted in 56 cases (57.14%). In 10 cases (10.20%) lymph node involvement by tumor, was not seen on macroscopic and microscopic examination. Out of 88 enlarged

lymph nodes from the axillary tail, 59 cases (60.20%) showed tumor deposits. 39 enlarged lymph nodes from the axillary tail, (39.79%) did not reveal any tumor deposits. The isolated lymph nodes were from 1 to 20. On an average, 08 lymph nodes were traced for histopathological examination. In one case, maximum number of enlarged lymph nodes from the axillary tail were 20 in which 18 lymph nodes showed tumor deposits.

## Discussion

A palpable breast lump is a common clinical problem that is presented to surgeons, gynaecologists, and general practitioners. Multidisciplinary approach is based on analyzing clinical and radiologic findings in conjunction with the pathologic features to diagnose the lesion and determine the best treatment plan for the patient. Breast cancer is a leading cause of mortality and morbidity among women worldwide with few cases being reported in men [2]. Developing countries have over the years enjoyed a reportedly low incidence of breast cancer; this picture is however changing due to adoption of a western lifestyle and better health seeking behavior of the populace. The high mortality associated with breast cancer is linked to the aggressiveness of the tumor which depends to a large extent on the histopathological subtypes. Several studies have pointed out the aggressiveness of breast cancer and some reports have attributed this to the genetic composition of the tumor and the histopathologic types. Many studies have tried to identify prognostic factors for breast cancer with nodal status and histopathologic subtypes featuring prominently as prognostic indices [7].

In the age group of 28-85 years of this study, about half of the female patients were aged 40-60 years. The mean age at diagnosis of breast cancer in females in this study was 56.5 years and agrees with the findings by researchers in other parts of developing countries. Kim-Mijung *et al* [8] observed a mean age at diagnosis to be 47.3 years. Lee AHS *et al* [9] observed an age range of 26 - 93 years with a median age of 58 years. Upper outer quadrant was most frequently involved (47.4%) in our study. Ackerman *et al* [10] also found that the upper outer quadrant was most frequently involved (50%) by malignant breast neoplasm. Majority of the cancers occurred in the right breast with our study and this agrees with the finding by Adeniji *et al* [11]. In the present study, the size of the neoplasm ranged from 1-9 cm. The mean size was 3.8 cms. Haagensen CD [12] reported a mean size of 3.4 cms. Established associations between reproductive

factors and the risk of breast cancer will mostly reflect associations with ductal tumors, which comprise about 80% of all breast cancer cases. Consistent with results from previous studies, our results indicated that the overall protective effect of a childbirth in relation to breast cancer risk may be particularly pronounced for mucinous tumors. Results from some previous studies have indicated that lobular tumors may be more strongly associated with age at first birth than other histological types of breast cancer [6].

The most common histopathological type of breast cancer found in this study was invasive ductal carcinoma, no special type (NST) accounting for 83.67% of cases. This agrees with the work of Ekanem et al of 75.5% in Benin [7]. Abudu et al from Ibadan reported a slightly higher figure of 94% [13]. These suggest that the predominant histopathological type of breast cancer in developing countries is the invasive ductal carcinoma NST. This explains the aggressive biological behavior of breast carcinoma found in developing countries women as reported by other researchers [14].

It is lamentable that there was no case of carcinoma in-situ in this study perhaps because of paucity of dedicated screening programmes for breast cancers. The least common histopathologic type in our series is the malignant phylloides tumour and signet ring cell carcinoma accounting for 1.02% of cases. This is in contrast with other studies which showed medullary carcinoma as the least common [15]. The design of this study being retrospective and the support of histochemical techniques will be helpful in typing of anaplastic tumours in a prospective multi-centred study and to better categorize breast cancers in developing countries. 98 cases of malignant breast neoplasms were graded according to the Nottingham modification of the Bloom Richardson grading system. Grade II invasive breast carcinoma was the most common (53.40%) (Figure 1).

This finding correlates with that of Truong PT *et al* (49.6%) [16]. The extent of tubule formation, number of mitotic figures and degree of nuclear pleomorphism are the important factors of Modified Bloom Richardson histological grading systems. The features like cellular arrangement, degree of cellular pleomorphism, degree of nuclear pleomorphism, and absence of myoepithelial cells are important to diagnose carcinoma on histopathology [17]. The degree of cell dissociation indicates cell cohesion status, to an extent to the degree of expression of the E-cadherin/catenin complex. Several studies showed that neoplasm with greater cell dissociation shows a higher incidence of regional lymph node metastasis (Fig 02) and lymphovascular invasion (Figure 3) [18]. A high degree of inflammatory infiltrate in tumor-surrounding tissue has also been noted. It has previously been suggested that inflammation-like processes in connection with the rebuilding of breast tissue after pregnancy and lactation may play a role for growth and spread of breast cancer tumors [19].

*Invasive Ductal Carcinoma, No Special Type (NST)*

This was the most common type of carcinoma occurring in 82 out of 98 cases reported accounting for an incidence of 83.67%. On gross examination, most tumors were hard to firm with irregular borders.

Microscopically, tumor cells displayed wide range of histologic appearances, like tubule formation, solid clusters, and ragged nests with mild to severe pleomorphic nuclei, atypical mitosis with tumor necrosis. Four of the neoplasms showed a mucinous component (<10%). Our finding correlates with Bane AL *et al* incidence of this type to 85% [20].

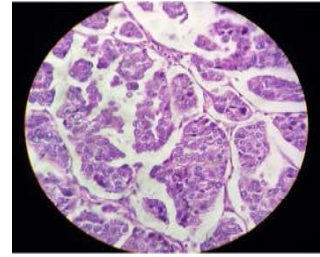


Fig. 1: Invasive breast carcinoma with cords, islands with tubular differentiation, moderate variability in size and shape, open vesicular nuclei, and visible nucleoli – Nottingham modification of the Bloom Richardson grading system II.



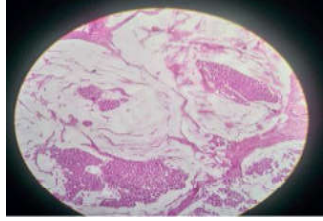
Fig. 2: Histopathological features showing lymph node metastasis in an invasive ductal carcinoma, No special type with subcapsular and multiple cortical infiltration.



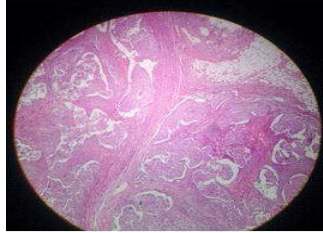
Fig. 3: Invasive ductal carcinoma: Histopathological features showing lymphovascular invasion by tumor cells

*Mucinous Carcinoma*

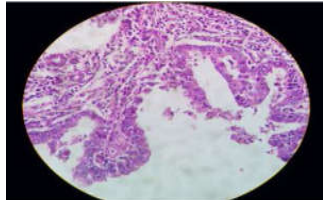
Two cases of mucinous carcinoma were reported, accounting for an incidence of 2.04%. Gross examination revealed soft consistency with gray-blue gelatin and had circumscribed borders. Histopathological examination showed clusters and island of tumor cells within large lakes of mucin (Figure 4). A similar



**Fig. 4:** Histopathological examination showing clusters and island of malignant tumor cells floating within large lakes of mucin in a case of mucinous carcinoma.



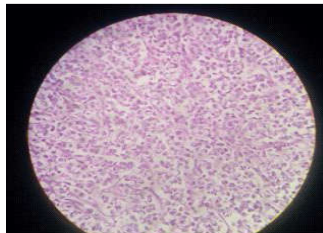
**Fig. 5:** The tumors cell arranged in syncytium like sheets of large cells with vesicular, pleomorphic nuclei in medullary carcinoma.



**Fig. 6:** Photomicrograph of intracystic papillary carcinoma: Malignant tumor cells, in dilated ducts arranged in papillary pattern of growth



**Fig. 7:** Tumor cells displayed dyscohesive infiltrating tumor cells arranged in single file or clusters with desmoplastic reaction (Indian file pattern)



**Fig. 8:** Tumor cells of signet ring cell carcinoma, showing signet ring cell features with cytoplasmic mucin and displacing the high grade nucleus to the periphery with presence of extracellular mucin

incidence of 1.67% was found in the study conducted by Baptist SJ *et al* [21]. The average age of the patients in the present study was 55 years. This finding correlates with that of Toikkanen S *et al* [22] who reported a mean age of 65 years.

#### *Medullary Carcinoma*

There were six cases (6.12%) of medullary carcinoma reported in the present study of all the malignant breast neoplasms. The tumors were soft, well circumscribed and showed syncytium like sheets of large cells with vesicular, pleomorphic nuclei with frequent atypical mitosis and lymphoplasmacytic infiltrate surrounding and within the tumor (Figure 5). Kapure *et al* [23] observed an incidence of 9.2%. The neoplasm fulfilled all the criteria for medullary carcinoma. Possibility of the diagnosis of atypical medullary carcinoma viz. a neoplasm with syncytial growth pattern but fulfilling only 2 - 3 criteria for medullary carcinoma, was ruled out since atypical medullary carcinoma carries a prognosis comparable to invasive ductal carcinoma, not otherwise specified [24].

#### *Invasive Papillary Carcinoma*

There was a single case of invasive papillary carcinoma in a 50 year old female (1.02%). Findings of the present study correlate with those of Haagensen CD [12] observed an incidence of 1.5%. Microscopically, the neoplasm showed few dilated ducts lined by a neoplasm cells arranged in papillary pattern of growth (Figure 6).

#### *Invasive Lobular Carcinoma*

Five cases of invasive lobular carcinoma were reported, accounting for 5.10% of the incidence among all malignant breast neoplasms. Microscopically, tumor cells displayed dyscohesive infiltrating tumor cells arranged in single file or clusters (Figure 7). The incidence found by Haque R *et al* was 1.05%. The neoplasm fulfilled all the criteria for medullary carcinoma [15]. In this case all the 14 axillary lymph nodes were involved by the neoplasm. Van Bogaert reported axillary lymph node metastasis in 63.6% of invasive lobular carcinoma [25]. In our study, no cases of male breast malignancies were reported. Most of the texts mention the incidence of male breast carcinoma to be less than 1% of all breast cancers [1].

#### *Signet Ring Cell Carcinoma*

One case of signet ring cell carcinoma showed, tumor cells arranged in diffuse sheets with majority showing signet ring cell features having high nuclear grade and tubular formation. Cytoplasm showed mucin, displacing the nucleus to the periphery. Focal areas also showed extracellular mucin (Figure 8).

### **Conclusion**

Invasive ductal carcinoma (NST) was the most common breast cancer in our study and this agrees with what is found in other parts of the country. The overall protective effect of a pregnancy seemed to be particularly pronounced in relation to mucinous tumors. Differentiation of breast cells after a full-term pregnancy, but also a long-term reduction in prolactin levels, have been suggested to explain the protective effect of a childbirth on the risk of breast cancer. Improved knowledge may have implications both for prevention and treatment of breast cancer disease. Because age 50 years is both the early-onset

mode and a valid menopausal surrogate, we further speculate that premenopausal exposures will have greater effect on early-onset than on late-onset breast cancers. Future population-based studies that include assessment of family history, breast cancer risk factors, environmental exposures, standardized histopathology review, and molecular characterization are needed to examine the conceptual framework of breast cancer model.

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