

Clinical and Histomorphological Profile of Breast Neoplasms

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Abstract

Introduction: Breast neoplasms have a high degree of heterogeneity under several distinct viewpoints such as variable clinical presentations, diverse morphological features, and different therapeutic responses. Understanding the clinical profile of breast cancer is important to develop early diagnosis efforts.

Aim: To evaluate clinical and pathological characteristics of breast neoplasms.

Materials and Methods: This study was conducted over a period of 2-year comprising 267 patients who underwent lumpectomy or modified radical mastectomy following a preliminary diagnosis on fine needle aspiration cytology or trucut biopsy specimens. The clinicopathologic evaluation was done in all of these cases following standard protocols.

Results: The study comprises 267 patients in the age range of 20-70 years. The majority of breast cancers occurred within the age range of 41-50 years with mean age of 45.5 years. Exceptionally one case of invasive ductal carcinoma was observed in the age 5 years. The most common benign tumor was fibroadenoma and in malignancy invasive ductal carcinoma was evident in 103 cases. Early menarche contributes to the major risk factor. Breast lump, nipple discharge, Peaud' orange appearance, and axillary lymphadenopathy are the common clinical presentations. Predilection toward the left side and location of lump over the upper outer quadrant has been documented. Most of the cases presented with American Joint Committee on cancer pathologic Stage II A.

Conclusion: This study gave an insight to the clinicopathological profile of breast cases in our area.

Key words: Breast neoplasms, Epidemiology, Histopathology cancer, Stage

INTRODUCTION

Breast neoplasms encompass a heterogeneous group of lesions that may be presenting as a palpable mass, non-palpable abnormality detected on imaging analysis or an incidental microscopic finding. They constitute a wide spectrum of histological lesions ranging from a benign tumor at one end approximating to carcinoma at the other end. Breast cancer is the most common cancer of women worldwide representing approximately 16% of all female cancer.¹ It represents the second leading cause of cancer

death among women after lung cancer.² In some of the studies, it occurs secondary to cervical cancer,^{3,4} presently 75,000 new cases occur in Indian women every year.⁵ Etiology of breast cancer is multifactorial. It includes diet, reproductive lifestyle, environmental and genetic factors.⁴ This study is intended to clarify the epidemiological and pathological features of breast cancer to adopt an adequate strategy of care in our area.

MATERIALS AND METHODS

A total number of 267 cases who attended the surgery outpatient department and for whom lumpectomy or modified radical mastectomy has been done were included in the study. Relevant clinical features such as age, parity, age of first childbirth, menstrual status, and family history were elicited. Location of lump, nodal enlargement, presence of nipple discharge, skin, and nipple changes were observed.

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The specimens were fixed in 10% formalin and usual techniques of histological processing, paraffin embedding, section cutting with microtome and hematoxylin and eosin staining were made. Histopathological evaluation was done with microscopy.

RESULTS

This study of breast neoplasms covers a total of 267 cases in which 120 cases were observed as benign and 147 cases as malignant neoplasms. The age range of patients was 20-70 with a median of 45 years.

As noted in Table 1, increased incidences of breast neoplasms were observed in 31-50 years (116 cases, 43.44%). The incidence is very low in pediatric age group <10 years (1 case, 0.37%) followed by 61-70 years (8 cases - 2.99%).

Bar diagram shows that benign lesions have a peak incidence in the age group of <20 years (55 cases - 45.84%) (Figure 1). Whereas malignancy reaches its peak in the age group 41-50 years (51 cases 34.93%). The findings of independent sample *t*-test are given in the following Table 2, which shows the difference in mean age between benign and malignant neoplasms.

Benign neoplasms occur at a relatively younger age than malignant neoplasms with statistical significance ($P < 0.001$). Clinical evaluation of malignant tumors is represented in Table 3.

All the cases presented with a breast lump. Risk factor like early menarche was seen in most cases (140 cases, 95.89%). Most of the women in our study were multiparous with a history of regular breastfeeding (141 cases, 96.57%). The tumor mostly involved the upper outer quadrant (85 cases, 58.21%) followed by diffuse involvement (36 cases 24.65%). Figure 2 illustrates the distribution of breast neoplasms. Malignant neoplasms predominate with (147 cases 54.66%) when compared with benign neoplasms (120 cases, 45.31%). Age incidence of individual benign neoplasms is given as shown in Table 4.

Most of the fibroadenomas are seen in the early reproductive age group, <20 years (53 cases, 50%) followed by 21-30 years (36 cases, 33.96%). Special forms of adenomas such as tubular adenoma and lactating adenoma were also observed in the same age group. One case of adenomyoepithelioma and myofibroblastoma was observed in the postmenopausal age group. Distribution of epithelial malignant tumors is shown in Table 5.

Table 1: Age incidence of breast neoplasms

Age group (years)	Number of cases (%)
<10	1 (0.37)
10-20	54 (20.22)
21-30	53 (19.85)
31-40	58 (21.72)
41-50	58 (21.72)
51-60	35 (13.10)
61-70	8 (2.99)
>70	-

Table 2: Comparison of mean age of benign and malignant neoplasms by independent samples

t-test

Variable	Age (Mean±SD)	<i>t</i> -test value	P value
Benign diseases	24.9±9.7	16.15	<0.001
Malignant diseases	45.3±10.7		

SD: Standard deviation

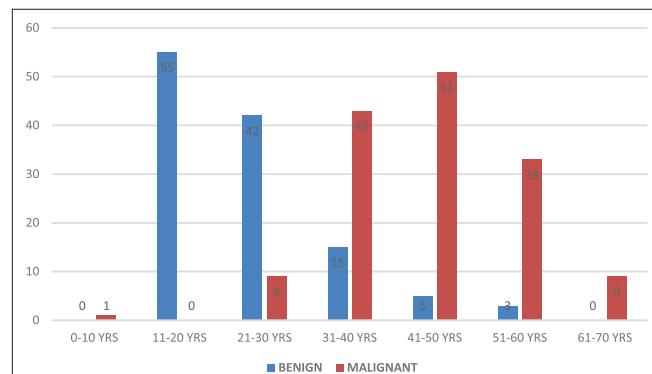


Figure 1: Comparison of age incidence of benign/malignant neoplasms

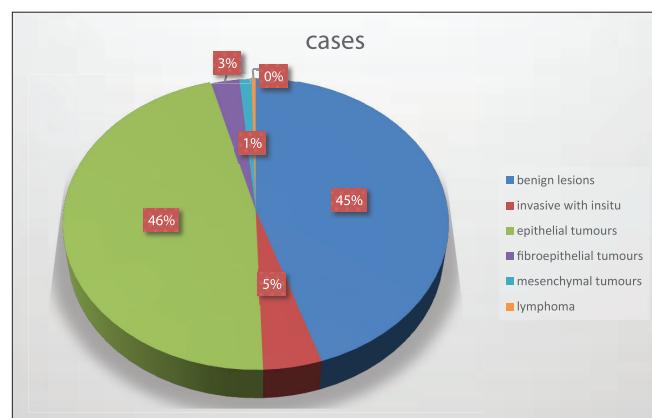


Figure 2: Distribution of breast neoplasms

Infiltrating ductal carcinoma (IDC) not otherwise specified (NOS) was observed as the most common malignant breast tumor (103 cases - 70.06%). Other fibroepithelial and non-epithelial malignant tumors of the breast that were observed are represented as shown in Table 6.

Table 3: Clinical evaluation of cases with malignant tumors

History/clinical features	Number of cases (%)
Early menarche	140 (95.89)
Age of first child birth	
Early	137 (93.83)
Late	9 (6.16)
Parous women	141 (96.57)
Nulliparous women	5 (3.42)
Breast fed	141 (96.57)
Menstrual status	
Menopausal	93 (63.69)
Menstruating	53 (36.30)
Family history	4 (2.73)
Treatment history	
Hormonal therapy	0 (0)
Previous biopsy for benign disease	2 (1.36)
Breast lump	146 (100)
Discharge	60 (41.09)
Skin changes	
Erythema	31 (21.23)
Peau de orange appearance	46 (31.50)
Ulceration	19 (13.01)
Nipple retraction	40 (27.39)
Axillary nodes	45 (30.82)
Location	
Upper outer quadrant	85 (58.21)
Upper inner quadrant	11 (7.53)
Lower outer quadrant	8 (5.47)
Lower inner quadrant	6 (4.10)
Diffuse-involving all quadrants	36 (24.65)

Table 4: Incidences of individual benign neoplasms

Type of benign neoplasm	Age groups				
	<20	21-30	31-40	41-50	51-60
Fibroadenoma	53	36	13	3	2
Fibroadenoma with benign phyllodes	1	3	-	-	-
Benign phyllodes	-	-	1	1	-
Others					
Nipple adenoma	-	1	-	-	-
Tubular adenoma	1	1	-	-	-
Lactating adenoma	-	1	-	-	-
Myofibroblastoma	-	-	-	1	-
Duct papilloma	-	-	1	-	-
Adenomyoepithelioma	-	-	-	-	1

DISCUSSION

Globally breast cancer is the most common cancer in females. Significant variations are noted in geographic, socio-demographic, and histomorphological profiles. International variations in incidence and mortality rates are a striking feature of breast cancer. Breast cancer is more common in Arab countries and in Malaysian women, but the incidence is higher in China and India compared to Malaysia. This difference could be due to reproductive, environmental, and dietary factors.⁶ Diomonde *et al.* in

Table 5: Distribution of epithelial malignant tumors

Type of tumor	Number of cases
IDC with DCIS	12
IDC-NOS	103
Invasive lobular carcinoma	2
Mucinous carcinoma	4
Medullary carcinoma	1
Invasive papillary carcinoma	5
Invasive micropapillary carcinoma	1
Infiltrating cribriform carcinoma	1
Adenoid cystic carcinoma	1
Neuroendocrine tumor	1
Metaplastic carcinoma	4
Adenomyoepithelioma with malignancy (epithelial)	1

IDC: Infiltrating ductal carcinoma, DCIS: Ductal carcinoma *in situ*, NOS: Not otherwise specified

Table 6: Distribution of fibroepithelial/non-epithelial malignant tumors

Type of tumor	Number of cases
Fibroepithelial	
Malignant phyllodes	7
Mesenchymal	
Pleomorphic sarcoma	1
Fibrosarcoma	1
Angiosarcoma	1
Lymphoma	
Non-Hodgkin lymphoma	1

their study of the evolution of cancer at Ivory Coast showed that cervical cancer was the first cancer of women followed by breast with a frequency of 10.52% of cases.⁴ As per Mohapatra *et al.*'s, hospital data from South India breast cancer constitutes 15.05% next to cervical cancer.³ In our study, the prevalence of breast cancer is 18.91% ranking second to cervical cancer in accordance. Contrary to this in metropolitan cities such as New Delhi, Mumbai, Ahamadabad, Kolkotta, and Trivandrum breast cancer takes the lead.³

The age-specific incidence of breast neoplasms ranges from 20 to 70 years and shows increased incidence in 31-50 years. Pertaining to benign neoplasms the mean age of incidence is 24.9 and for malignant lesions, it is 45.3. This is comparable with the studies of Ranabhat *et al.*⁷

In a study conducted at Nepal,⁷ proportion of breast diseases was found to be 90.04% benign neoplasms and malignancy as 8.8%, whereas in our study they are almost equal comprising benign neoplasms to be 44.94% and malignancy 55.05%. Studies from Nepal, Lahore, Aurangabad, Mumbai,⁷ and Malawi,⁸ have found fibroadenoma as the most common benign breast lesion. In our study, fibroadenoma constitutes 89.16% with the peak incidence in the age group of <20 years. Next stands the

phyllodes tumor comprising 4.86% of mammary neoplasms in contrast to the literatures where phyllodes tumor accounts for <1% of all mammary neoplasms.⁹ Malignant transformation has been observed in 7 cases, of which 3 showed heterologous differentiation of liposarcoma, chondrosarcoma and rhabdomyosarcoma. Special types of adenoma-like tubular adenoma and lactating adenoma were observed. Myoepithelial tumors exhibit a wide variety of patterns making it difficult to distinguish from other benign entities. Hence, the diagnosis of adenomyoepithelioma is restricted to cases falling outside the spectrum of well recognized common benign conditions. One case of adenomyoepithelioma and myofibroblastoma also have been reported. Breast cancer in women below 50 years constitutes 34.93% followed by 29.45% and 6.12% below 40 and 30 years of age, respectively. Premenopausal and perimenopausal incidence are reported in Indian^{6,10,11} other Asian^{7,12} and African countries.^{8,13} In contrast, studies of Shirley *et al.*,¹⁴ Western,³ and Australian¹⁵ literatures depict the predominant postmenopausal occurrence. These results point toward racial differences in the molecular profiles of breast carcinoma.¹⁴ The incidence of breast carcinoma in males was found to be 1.3-1.7% in some of the studies^{3,10} but to the contrary no male case has been reported in our study.

The risk factor evaluation shows history of early menarche in almost all cases in accordance with the literature¹⁰ supporting the higher risk. Although nulliparity and low parity are associated with increased risk, in our study, the majority of patients are multiparous. Higher the parity higher is the association with triple-negative cancers¹³ as it is not responsive to sex hormones associated with parity. Norway studies¹⁶ report a high protective effect for women with early age of the first childbirth which is in contrast with our study where early age at first childbirth contributes to 93.83% of cases. Exclusive breastfeeding long practiced in developing countries reduces breast cancer through resting ovaries.¹ In the contrary in our study, 96.57% of them have breastfed. Raina *et al.*,¹⁷ noticed 7% patients with breast cancer in first degree relatives. Similarly, 8.78% has been observed in Ivory Coast.¹ Rosen *et al.*¹⁸ observed 31% followed by Siguan *et al.*¹² 27%. Familial breast cancers are not a significant entity in our series (2.72%). Advanced Western Nations have undergone a dramatic evolution in the diagnosis of breast cancer since mid-1980's. Subsequent to the widespread availability of mammographic screening, the diagnosis of clinically occult and non-palpable lesions is on the rising trend. In our study, women with breast cancer almost all detected their disease by themselves after finding a lump in breast emphasizing the need to educate women on self-breast examination. On viewing, the clinical scenario the incidence of breast carcinoma was documented on left side (62.54%) and in the upper

outer quadrant (58.21%) corroborating with previous reports.^{10,12,19} The possible explanations are that left breast is bulkier and upper outer quadrant has a relatively large volume of breast tissue.¹⁰ Preponderance of right side is noted in some studies reflecting the ethnic variation in population.^{6,7} As per studies of Raina *et al.*,¹⁷ nipple discharge was present in 4.9% of patients whereas in our study it constitutes 41.09% of patients. Other nipple and skin changes are comparable with other available studies.

Regarding the histological types, IDC is the most common and is supported by other studies.^{17,19} To our amazement a significant observation in our study is the incidence of IDC in a 5-year-old girl possibly as a consequence of genetic mutations. In most of the studies, lobular carcinoma^{6,17,19} occupies the second place whereas in our study invasive papillary carcinoma (3.4%) is followed by mucinous carcinoma (2.72%) and metaplastic carcinoma (2.72%). Mucinous and papillary tumors predominate in the Jamaican studies,¹⁴ In contrast to other studies³ metaplastic carcinoma occupies a significant position in our study, interestingly metaplastic carcinoma with squamous and osteosarcomatous differentiation are evident. Intratumor heterogeneity underpinned by distinct genetic alterations paves way for morphological diversity with carcinoma and sarcoma at either ends of the spectrum. Regarding prognosis, anecdotal evidence suggests early recurrence and poor survival; they are triple negative tumors limiting potential systemic treatment.⁹ Newer variants, invasive cribriform carcinoma, invasive micropapillary carcinoma, adenoid cystic carcinoma, and neuroendocrine tumor each contribute to 0.68%. Although these percentages are comparatively low, recognition of them is important as prognostic significance is there.

Breast is a rare site for a primary sarcoma. It needs diligent sampling to exclude focal evidence of biphasic epithelial or sarcomatous differentiation to rule out phyllodes and metaplastic carcinoma. 3 rare cases of fibrosacroma, pleomorphic sarcoma, and angiosarcoma have been documented. Primary angiosarcoma of breast though rare is the most common pure malignant stromal tumor of the breast. Radiation-induced sarcomas are well recognized and estimated to be 0.1%.⁹ The interval between radiation exposure and development of angiosarcoma is usually between 2 and 10 years. Post-radiation angiosarcomas are more common than de nova angiosarcoma and that too particularly in therapy of older women. Angiosarcoma noted in our study does not have any history of exposure to radiation. Kaposi sarcoma predominates in Ivory Coast probably due to the impact of the HIV virus in their society.¹ Primary breast lymphoma is a rare clinical entity that accounts for <1% of all patients with Non-Hodgkin's lymphoma. We have come across a case of primary B-cell

lymphoma of breast. The incidence of B-lymphoma is high in Sub-Saharan African countries probably an endemic Burkitt lymphoma; the spreading of tumor cells from an unknown site to the mammary vessels could be thought of.¹ WHO stated that there are marked variations in the size ranging from under 10 mm to over 10 mm.¹⁹ Recording the measurements of size, T1 <2 cm constitutes 2.4% and 85.36% and 12.24%, respectively, for T2 and T3 in our study. African literatures¹³ report the presentation of tumor with stage III or IV in contrary to our study where stage II presentation is the most common.

Nodal positivity portends the worst prognosis. The 10 years survival rate is 70-80% with node-negative carcinoma, 35-40% in carcinoma with 1-3 positive nodes and 10-15% in patients with more than 10 nodes.³ Nodal positivity was noted in 29.93% of cases in contrast to studies of Amr *et al.*¹¹ which showed positivity in 61.7% of

cases. 21.76% of cases show <3 nodes positive and 8.16% have more than 3 nodes positivity.

Immunohistochemistry served as an adjunct tool for diagnosis of difficult cases. Smooth muscle actin shows positivity in a case of adenomyoepithelioma with suspicious malignancy (Figure 3a and b). Myoglobin positivity is observed in a case of malignant phyllodes with rhabdomyosarcomatous differentiation (Figure 4a and b) and a case of lymphoma was confirmed with CD 20 positivity (Figure 5a and b).

CONCLUSION

Breast cancer is the most common cancer in females posing a major health problem. There is a need for expedient evaluation of breast masses with an improved clinical and pathological characterization. The burden of breast cancer has to be brought down toward a declining trend. Hence, there is an urgent need to increase population screening program for early detection, training of women (breast self-examination), health worker, and medical practitioners. At present mammography serves as a screening tool but is less likely to be effective due to its insensitivity in high-density breast tissue at younger age. Moreover, most patients in our set up are unable to afford mammography due to their poor socio-economic background. Thus, there is a need for poverty alleviation programs, improved accessible and affordable health-care delivery services.

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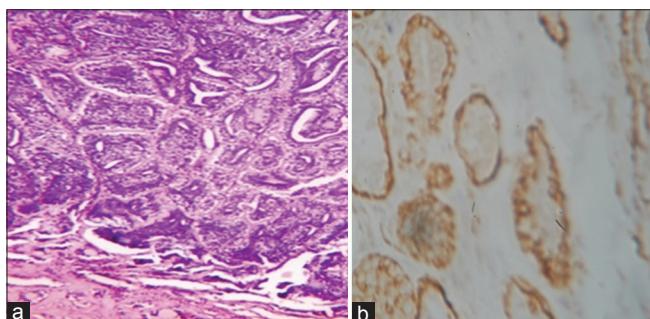


Figure 3: (a) Adenomyoepithelioma shows tubules lined by epithelial and myoepithelial cells. (b) Smooth muscle actin positivity

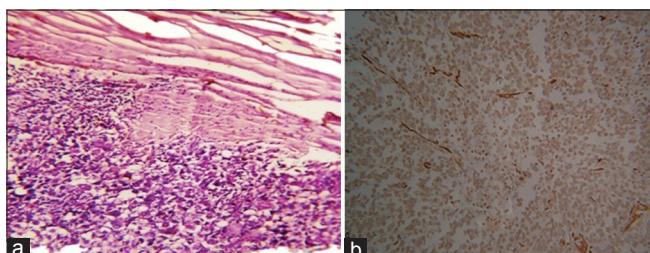


Figure 4: (a) Malignant phyllodes with rhabdomyoblastic, (b) myoglobin positivity of differentiation rhabdomyoblasts

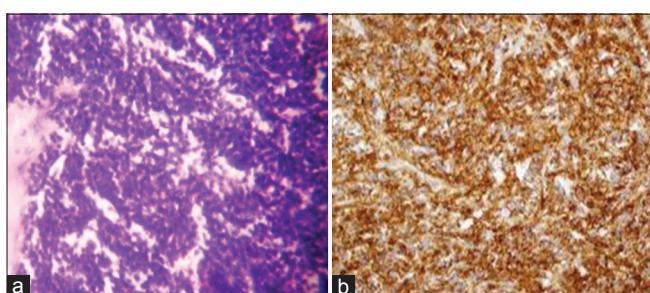


Figure 5: (a) Lymphoma showing sheets of (b) CD 20 positivity monotonous cells interspersed with blasts

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