# Clinico-pathological study of breast carcinoma: A prospective two-year study in a tertiary care hospital

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# ABSTRACT

**Background:** Breast cancer is the most frequent cancer in female, both in developed and developing regions, and ranks second overall next only to lung cancers. International variation in both incidence and mortality is one of the most striking features of breast cancer. **Aims:** To assess the clinical profile of the patients of breast carcinoma as well as relevant macroscopic and microscopic features of the mastectomy specimens. **Materials and Methods:** The present prospective study was carried out on clinically suspected and pre-operative FNAC-confirmed 120 cases of breast carcinoma who were admitted in the department of surgery for mastectomy during the study period of two years. In addition to relevant clinical features, macroscopic and microscopic features of mastectomy specimens were noted. **Results:** Mean age of the study population was 46.53 years. Most of the patients presented with breast lump with or without other features. Mean tumor size in the study population was 5.91 cm with standard deviation  $\pm$  2.59. Most of the cases (90.8%; 109 cases out of 120 cases) were diagnosed as IDC, NOS (Infiltrating ductal carcinoma, not otherwise specified). Mostly (62 cases; 51.7%), we got the histological grade 3 tumors. Lympho-vascular invasion was identified in 25.8% cases (31 cases out of 120 cases). Skin and nipple areola was involved in 15.0% cases (18 cases). **Conclusion:** IDC, NOS is the most common histologic type of breast cancer in our study population. Most commonly affected age group by breast cancer is 35-50 years. In most of the cases, size of the mass was more than 5 cm involving multiple quadrants of breast and with positive lymph nodes. Histologically, grade 3 tumor is most prevalent in this population.

Key words: Breast carcinoma, grade, invasive ductal carcinoma, not otherwise specified, prognosis

# INTRODUCTION

Breast cancer is by far the most frequent cancer in female, both in developed and developing regions, and ranks second overall next only to lung cancers.<sup>[1]</sup> Mortality rates from breast cancer have increased during the past 60 years in every country. International variation in both incidence and mortality is one of the most striking features of breast cancer.<sup>[2]</sup> The age-standardized rates of breast cancer in India are significantly lower, almost

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one quarter to one-third of those in North America and Europe, respectively.<sup>[3]</sup> The postulated reasons for the lower incidence of this disease are believed to be lower socio-economic status, delayed menarche (14 years vs. 12.6 years in white women), relatively early age at birth of first child, high parity, and nearly universal and prolonged breast-feeding.<sup>[4]</sup> The triple approach to the diagnosis of breast carcinoma, involving clinical examination, imaging (mammography), and fine needle aspiration cytology, has an accepted place in the assessment of patients presenting with solid breast mass.<sup>[5,6]</sup> The traditional pathological factors of lymph node status, tumor size, histological type, and histological grade are the most useful prognostic factors in breast cancer patients.<sup>[7]</sup>

We have conducted the study to assess the clinical profile of the patients of breast carcinoma as well as relevant macroscopic and microscopic features of the mastectomy specimens.

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### MATERIALS AND METHODS

The present single-center, prospective, cross-sectional study was carried out on 120 cases of breast carcinoma after obtaining the proper approval from ethical committee of the institution and informed consent from the patients. All the clinically suspected and pre-operative FNAC (fine needle aspiration cytology)-confirmed patients of breast cancer, who were admitted in the department of surgery for mastectomy in our institution during the study period of 2 years (01.11.2008-31.10.2010), were included in the study. The patients with breast carcinoma, who attended the surgery OPD but not admitted in the department of general surgery for mastectomy in the study period, patients having history of pre-operative chemotherapy or radiotherapy for breast carcinoma, and male patient with breast carcinoma, were excluded from the study.

Relevant clinical features like age, laterality of the tumor, mode of presentation, menstrual and reproductive history, history of breast cancer in 1<sup>st</sup> degree relative, fixity of the tumor and skin, and nipple-areola changes were assessed. Size, number, and location of tumor in mastectomy specimens were noted macroscopically. Microscopically, histological type, histological grade by Nottingham modification of Scarff Bloom Richardson (SBR)'s method, lymphatic and blood vessel invasion, and lymph node involvement were evaluated in Hematoxylin and Eosin (H and E)-stained sections. Histology procedure: After doing primary slicing of the mastectomy specimen on the first day, recommended sections were taken on the second day of receiving the specimen. The tissues were then processed following the routine steps of dehydration in ethyl alcohol, clearing in Xylene, and impregnation with paraffin. The processed tissues were embedded in paraffin wax. Sections were cut at 3-5 µm thickness and stained with Hematoxylin and Eosin (H and E) stain. Mitotic figures were scored using an Olympus CH20i microscope with field of view number 18 and high power field diameter 0.45 mm.

All the statistical analyzes were done using IBM SPSS statistics software, version 19.

### RESULTS

Clinical features, menstrual and reproductive history, macroscopic and microscopic features are clearly depicted in Tables 1-4 and Figures 1 and 2. Mean age of the study population was 46.53 years, and most of the cases were clustered in 35 to 50 year age group [Table 1]. Most of the patients presented with breast lump with or without other features, and nipple retraction was a very common finding. The tumor mass mostly fixed to the deeper structures. Bilateral breast involvement was observed only in two cases of invasive lobular carcinoma.

Mean age of menarche was 12.17 years, and patients mostly

Table 1: Clinical features of the	breast carcinoma patients		
Clinical features		No. of cases	Percentage
Age (years)			
	<35	10	8.3
Mean=46.53	35-50	77	64.2
Standard deviation=11.85	51-60	17	14.2
	>60	16	13.3
Laterality			
	Right	62	51.7
	Left	56	46.7
	Bilateral	2	1.7
Mode of presentation			
	Lump (only)	79	65.8
	Lump+Pain	21	17.5
	Lump+Nipple changes	14	11.7
	Lump+Skin changes	6	5.0
Fixity	1 0		
	Deeper structures only	68	56.7
	Skin only	0	0.0
	Deeper structures and skin	20	16.7
	Free	32	26.7
Skin and Nipple-areola changes			
	No change	34	28.3
	Retraction only	29	24.2
	Peau d' orange only	4	3.3
	Retraction and Peau d' orange	37	30.8
	Retraction and discharge	6	5.0
	Retraction, Peau d' orange, and discharge	4	3.3
	Retraction, Peau d' orange, and ulceration	4	3.3
	Retraction, Peau d' orange, and fungation	2	1.7

Table 2: Menstrual and reproductive history of the   patients			
Menstrual and reproductive history	No. of cases	Percentage	
Age of menarche (years)			
Mean=12.17 ≤13	99	82.5	
Standard ≥14	21	17.5	
deviation=1.27			
Parity			
Unmarried	19	15.8	
Nil	11	9.2	
1-2	53	44.2	
3-4	33	27.5	
≥5	4	3.3	
Age of first childbirth (years)			
Nulliparous (Married+	30	25.0	
Unmarried)			
≤19	35	29.2	
20-24	39	32.5	
≥25	16	13.3	
Age of menopause (years)			
Pre-menopausal	50	41.7	
≤44	42	35.0	
≥45	28	23.3	

had the 1 to 2 children (44.2%). Out of 120 patients, 50 (41.7%) were pre-menopausal and rests (70 patients, 58.3%) were post-menopausal [Table 2]. Only 8 patients (6.7%) had the positive family history of breast cancer in first degree relatives.

Mean tumor size in the study population was 5.91 cm with standard deviation  $\pm$  2.59 [Table 3]. Majority of the cases in this study population i.e., 54 cases (45.0%) had diffuse involvement of the breast. Among the tumors with single quadrant involvement, frequency of occurrence was maximum in the upper outer quadrant (15.8%) followed by central region (14.2%).

Most of the cases (90.8%; 109 cases out of 120 cases) were diagnosed as IDC, NOS (Infiltrating ductal carcinoma, not otherwise specified) [Table 4]. Mostly (62 cases; 51.7%), we got the histological grade 3 tumors [Figure 1a]. Lympho-vascular invasion [Figure 2a] was identified in 25.8% cases (31 cases out of 120 cases). Lymph nodes were involved [Figure 2b] in 57.5% cases (69 cases out of 120 cases). Skin and nipple areola was involved in 15.0% cases (18 cases). Type of skin and nipple areola involvement was classified according to recommended protocol.[8]

# **DISCUSSION**

According to Fletcher's textbook,<sup>[9]</sup> breast cancer can occur at any age, but rare in patients younger than 25 years and over 80 years; the peak incidence is between 45 and 60 years. A very large and well-known study on trends of breast cancer in Arab countries showed median age at presentation at around 50 years as compared to 63 years in industrialized Table 3: Macroscopic features noted in the mastectomy specimens

specificits			
Macroscopic feature	S	No. of cases ( <i>n</i> =120)	Percentage
Size (cm) Mean=5.91 Standard deviation=2.59 Maximum=13.5 Minimum=1.9 Range=11.6 No. of mass	≤1.0 1.1-2.0 2.1-5.0 ≥5.1	0 2 41 77	0.0 1.7 34.2 64.2
Location (quadrant)	1 2 3	107 11 2	89.2 9.2 1.7
	Diffuse Central Upper outer quadrant Upper inner quadrant	54 17 19 14	45.0 14.2 15.8 11.7
	Lower outer quadrant Lower inner quadrant	7 9	5.8 7.5

nations, and breast cancer came out as most common cancer among women in Arab countries.<sup>[10]</sup> Breast cancer is the commonest cancer in Malaysian women. The incidence is higher in Chinese and Indian women compared to Malay women, and this difference could be due to reproductive, environmental, and dietary factors. The commonest age at presentation is between 40-49 years, with just over 50% of the cases under the age of 50 years, 16.8% below 40, and 2% under 30 years. Women in Malaysia, especially Malay women, present at later stages and with larger tumors compared to their western counterparts. Consequently, the survival in Malay women is worse than with Chinese and Indian women.<sup>[11,12]</sup> Hence, in this study, the age group for peak frequency of occurrence of breast cancer corroborated with the findings of most of the studies conducted in Asian countries.

There is a slightly higher frequency of invasive breast cancer in the left breast with a reported left to right ratio of approximately 1.07 to 1 in WHO literature, and an 8-19% incidence of contra-lateral tumors is seen in case of invasive lobular carcinoma.<sup>[7]</sup> Both breasts were affected almost equally by carcinoma in Saudi Arab females. Involvement of the right breast was seen in 64 cases (46.7%), the left breast in 67 (48.9%), and both breasts in one case only, which was lobular carcinoma histologically.<sup>[13]</sup> A study in Kuwait revealed that right and left breasts were involved by cancer in 53.6% and 42.2% cases, respectively, and both breasts were involved in rest of the cases.[14] The slight preponderance of carcinoma in right breast in respect to

Table 4: Microscopic features observed in the mastectomy   specimens				
Microscopic features	No. of cases ( <i>n</i> =120)	Percentage		
Histological type				
IDC, NOS	109	90.8		
Lobular	6	5.0		
Mucinous	2	1.7		
Medullary	1	0.8		
Tubular	1	0.8		
Invasive papillary	1	0.8		
Histological grade	0	17		
Grade 1 Grade 2	8 50	6.7 41.7		
Grade 2 Grade 3	62	51.7		
Lymphatic and blood vessel in		51.7		
Present	31	25.8		
Absent	89	74.2		
Lymph node involvement	07	7 1.2		
Involved	69	57.5		
Not involved	51	42.5		
No. of involved lymph nodes				
Negative	51	42.5		
1-3	29	24.2		
≥4	40	33.3		
Skin and nipple-areola involve				
Involved	18	15.0		
Not involved	102	85.0		
Type of Skin and nipple-areol				
Not involved	102	85.0		
Paget disease of	2	1.7		
the nipple Direct invasion	4	FO		
	6	5.0		
into Dermis and				
Epidermis without ulceration				
Direct invasion	6	5.0		
into Dermis and	0	5.0		
Epidermis with				
Skin ulceration				
Ipsilateral	4	3.3		
Satellite Skin	т	0.0		
nodule±Lymph				
vascular invasion				
Diffuse Dermal	0	0.0		
Lymph vascular	v	0.0		
invasion with				
clinical features				
of Inflammatory				
carcinoma				
IDC: Invasive duetal careinama, NOS	- Not otherwise encoified			

IDC: Invasive ductal carcinoma, NOS: Not otherwise specified

left breast is just a variation within normal limit in our study with small sample size, or it might be due to ethnic variation of the population in this region, which needs further long-term study.

Frequencies of symptoms in breast carcinoma reported by WHO are 60-70% for breast lump, 14-18% for pain, 7-9% for nipple problems, 1% for deformity, 1% for inflammation.<sup>[7]</sup> In a study by Raina, *et al.*<sup>[15]</sup>, most of the patients i.e., 96.5% presented with breast lump. 15.8% patients had pain, and 4.9% had nipple discharge in addition. Mode of presentation of the patients in the present study shows almost similar picture of the other studies.

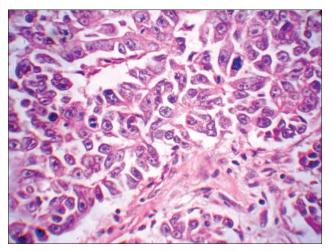


Figure 1: (a) Grade 3 invasive ductal carcinoma, not otherwise specified with prominent nucleoli and mitotic figures. (H and E,  $\times$ 400)

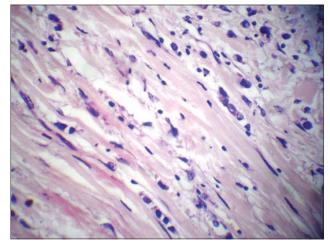


Figure 1: (b) Invasive lobular carcinoma showing "Indian file" pattern of cell distribution (H and E,  $\times400)$ 

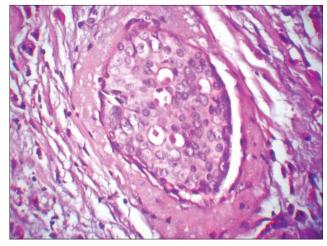


Figure 2: (a) Vascular invasion in invasive ductal carcinoma, not otherwise specified. (H and E,  $\times 400)$ 

In a large study in AIIMS, New Delhi showed 49.7% women were pre-menopausal, 48.5% post-menopausal. Median ages of menarche and menopause were 14 years

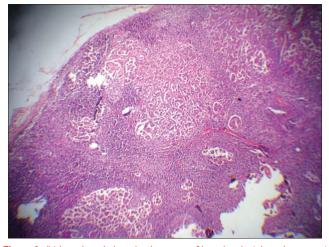


Figure 2: (b) Lymph node invasion in a case of invasive ductal carcinoma, not otherwise specifie. (H and E,  $\times 40)$ 

(range 12-17 years) and 46 years (range 36-56 years), respectively.<sup>[15]</sup> Amr, *et al.*<sup>[13]</sup> found 60% patients in pre-menopausal age group and 40% in post-menopausal age group in a large retrospective study.

Raina, *et al.*<sup>[15]</sup> noticed 7% patients with history of breast cancer in first degree relative. Rosen *et al.*<sup>[16]</sup> observed 31% of the patients reported with one or more relatives who were known to have had breast cancer in a study on 1024 patients.

Meena, *et al*.<sup>[17]</sup> observed that 58% of the breast lumps were freely mobile while remaining were fixed. There is an inadequacy of the data in recent literature regarding this parameter.

Nipple retraction was present in 43% of the cases, Peau d' orange appearance in 18% of the cases, and ulceration of the skin in 13% of cases in the study by Meena *et al.*<sup>[17]</sup> The findings of this study are comparable with that of other available studies.

The study conducted in Singapore general hospital on the patients aged 35 years or younger revealed the tumor size in 80 cases with values ranging from 0.3 to 11.5 cm (mean 2.7 cm, median 2.1 cm). Of these, 16 (20%) cases were  $\leq$  2 cm (T1), 48 (60%) were 2-5 cm (T2), 14 (17.5%) measured from above 5 cm to 10 cm (T3), and two cases (2.5%) were more than 10 cm in maximum dimension.<sup>[18]</sup> Of 97 cases with recorded measurements of the size of the tumor, 36 cases (37.1%) were less than 2.5 cm in maximum diameter, and 61 cases (62.9%) were more than 2.5 cm in a large study in Saudi Arab.<sup>[13]</sup> But, these variations can be concluded by the fact as stated by WHO is that there are marked variations in the size from under 10 mm to over 100 mm.<sup>[7]</sup>

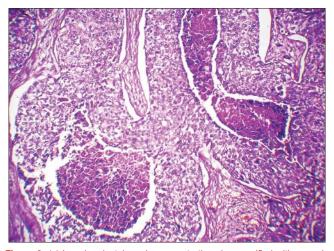


Figure 2: (c) Invasive ductal carcinoma, not otherwise specified with comedo necrosis (H and E,  $\times 100)$ 

According to WHO literature, 40-50% of the tumors occur in the upper outer quadrant, and there is a decreasing order of frequency in the other quadrants from the central, upper inner, lower outer to the lower inner quadrant.<sup>[7]</sup> Baily Love's textbook<sup>[19]</sup> says breast cancer most frequently involves the upper outer quadrant (60%) followed by 12% in both central zone and upper inner quadrant, 10% in lower outer quadrant, 6% in lower inner quadrant. The lump was found in upper outer quadrant in 54% cases followed by lower outer quadrant (12%), lower inner quadrant (12%), upper inner quadrant (5%), and central (7%) and diffuse (10%) in a study conducted in SMS medical college, Jaipur.<sup>[17]</sup>

The discrepancies of probably arouse due to two reasons. Most of the reported series are from countries where breast cancer screening is a routine procedure, and early detection is usual in contrast to this study population in which screening has not yet been implemented. Lack of awareness and poor socio-economic status also compelled the patients to come at later stage with larger tumor involving multiple quadrants.

WHO stated IDC, NOS is the most common type of invasive carcinoma in breast comprising between 40% and 75% in different published series followed by invasive lobular carcinoma in 5-15% cases.<sup>[7]</sup> In all the large studies by Rosen, *et al.*<sup>[20]</sup>, Ellis, *et al.*<sup>[21]</sup>, Page and Anderson<sup>[22]</sup>, IDC, NOS came out as the most common invasive carcinoma of the breast followed by invasive lobular carcinoma. Raina, *et al.*<sup>[15]</sup> observed invasive ductal carcinoma in most (92.8%) of the patients followed by invasive lobular carcinoma (2.9%) and medullary carcinoma (1.4%).

Histological subtyping in a study in Singapore disclosed 92.3% ductal, 2.2% lobular, 2.2% mucinous, 2.2% atypical

medullary, and 1.1% with both ductal and lobular features in 91 patients with invasive carcinomas.<sup>[18]</sup> The distribution of histological types of breast carcinoma in this study population is almost similar to that of other reported series.

Pinder, *et al.*<sup>[23]</sup> observed definite vascular invasion in 22.8% of cases, and concurrence between pathologists was high in this study. Vascular invasion was strongly associated with lymph node stage, tumor size, histological grade, and type of tumor. Vascular invasion was proved as independent prognostic factor for both survival and for local recurrence of tumor.

Lymphatic vessel invasion was present in 34.2% of cases, and blood vessel invasion in 4.2% cases in a study in Italy. Lymphatic vessel invasion correlated with blood vessel invasion, and both were correlated with metastatic axillary lymph nodes and increasing tumor size and grade.<sup>[24]</sup>

The frequency of lympho-vascular invasion in the present study (25.8%) appears to be more or less similar to the reported frequency in several other studies.

In a large study by Amr, *et al.*<sup>[13]</sup>, 81 patients out of 137 underwent mastectomy with axillary lymphadenectomy. Thirty-one cases (38.3%) had negative lymph nodes for metastatic deposits, and 50 cases (61.7%) had positive lymph nodes. Of the latter group, 17 cases (21%) had metastases in one to three lymph nodes and 33 cases (40.7%) in more than three lymph nodes.

The study by NSABP (National Surgical Adjuvant Breast and Bowel Project) on 505 patients with primary breast cancer with histologically proven positive lymph nodes observed the relationship between the number of positive lymph nodes and 5-year disease-free survival. The disease-free survival (DFS) of the lymph node negative cases was 85%, and single node positive cases were 63%. Greater numbers of involved nodes were associated with a progressively worse prognosis. They established the validity of previous observations, indicating the appropriateness of grouping primary breast cancer patients into those with negative, 1 to 3, or  $\geq$ 4 positive nodes.<sup>[25]</sup>

Khan, *et al.*<sup>[26]</sup> observed the overall frequency of nipple-areola involvement in 19.1% cases (26 cases out of 136). The frequencies of occurrence of Paget's disease and direct malignant invasion were 2.94% (4 cases) and 16.17% (22 cases), respectively.

In 15 cases (11%) out of 137 cases, the tumor attained quite a large size and was associated with ulceration of the skin with formation of a fungating mass. Three cases exhibited massive nipple involvement by direct extension from underlying tumor. Four more patients showed clinical and histological features of involvement of the nipple by Paget disease, one associated with intra-ductal carcinoma, and the rest involved with infiltrating ductal carcinoma.<sup>[13]</sup> The observations of this study are comparable to the other contemporary studies.

The largest and most well-known study on histological grading by Elston and Ellis<sup>[27]</sup> found 342 cases (19%) of grade 1, 631 cases (34%) of grade 2, and 857 cases (47%) of grade 3 tumors. Another very well-known and large long-term follow up study was performed by Rakha, *et al.*<sup>[28]</sup> on 2,219 cases in Nottingham, UK. In this study, 18.6% were grade 1, 35.6% were grade 2, and 45.6% were grade 3 breast cancers. Data on the pathology of breast cancer in Asian women revealed a pattern of a higher proportion of patients with high tumor grade (grade 3 of the Bloom and Richardson grading system), and hormone receptor-negative tumors.<sup>[29]</sup>

In the present study, we got more cases of grade 2 and grade 3 tumors and very few cases of grade 1 tumors. This interesting finding could be due to two reasons. Either higher grade of the tumors are more common in this population, or it might be due to grade progression as a consequence of late presentation.

# CONCLUSION

Invasive ductal carcinoma (IDC), not otherwise specified (NOS), is the most common histologic type of breast cancer in our study population. Its frequency of occurrence far exceeds that of the other histological types. Most commonly affected age group by breast cancer is 35-50 years, and most of the patients are from post-menopausal age group. In most of the cases, size of the mass was more than 5 cm involving multiple quadrants of breast and with positive lymph nodes. Histologically, grade 3 tumor is most prevalent in this population. Occurrence of grade 1 tumor is very infrequent.

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