

# Clinico-Pathological Characteristics of Breast Carcinoma at A Tertiary Care Center in Bangladesh

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## ABSTRACT

**Background:** Breast carcinoma is the most common malignant neoplasm and the leading cause of death from cancer in women. Nottingham Grading System (NGS) is a widely used histological grading system of breast cancer, which has some prognostic relevance. This study was undertaken to evaluate both histological grade and the clinico-morphological profile of breast cancer patients in a tertiary care center in Chattogram region in Bangladesh.

**Materials and methods:** This prospective study was carried out on fifty histologically diagnosed cases of breast carcinoma. All were graded according to Nottingham Grading System (NGS). Clinico-morphological profiles of all cases were recorded methodically and these were distributed according to Nottingham Grading System (NGS). Fifty patients' ages ranged from 24 to 75 years with a mean of 46.52 years were included in study.

**Results:** Of 50 cases, 17 (34%) 31 (62%) and 02 (04%) cases were graded as grade I, II and III by histological grading. Right breast (62%) was more commonly involved. Out of 42 lesions with 02- 05 cm size, 26 (61.9%) lesions were grade II. Out of 07 lesions with peau d' orange, 05 (71.4%) lesions were grade II and 01 (14.2%) lesion was grade III. Among 08 lesions with puckered skin, 07 (87.5%) lesions were grade II. Out of 19 cases with metastatic lymph node, 10 (52.6%) cases were grade II.

**Conclusion:** Patients with high grade tumors have aggressive clinical and morphological presentations. So histological grading using Nottingham Grading System (NGS) has a prognostic relevance with a breast cancer patient.

**Key words:** Breast carcinoma; NGS; Clinical profile.

## INTRODUCTION

Carcinoma of the breast is the most common non-skin malignancy in women. A woman who lives up to 90 years has one eighth chance of developing breast cancer<sup>1</sup>. The

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incidence and clinical presentation of breast cancer vary in different geographic areas<sup>2</sup>. In some regions of the world (North America, Western Europe and Australia) breast cancer mortality is finally beginning to fall, because of earlier diagnosis and improved therapy. But countries with traditionally low incidence are now experiencing some what increasing trend<sup>3</sup>.

In Bangladesh, patients suffering from breast cancer have been increasing. Because of the existing social circumstances, the tendency to overlook and also for the hesitation to be examined, they are reporting advanced stage of malignancy<sup>4</sup>.

Again, the three strongest prognostic determinants in operable breast cancer used in routine clinical practice internationally are lymph node stage, primary tumor size and tumor histologic grade. The most widely used histologic grading system of breast cancer is the 'Elston and Ellis' Modified Bloom-Richardson (MBR) grading system also known as the Nottingham Grading System (NGS)<sup>5</sup>. The

prognostic relevance of NGS has been demonstrated in multiple independent studies and it has been recommended by various professional bodies internationally (WHO, American Joint Commission on Cancer [AJCC] European Union [EU] and UKRCPATH)<sup>6</sup>.

Now, the present study is designed to study clinco-morphological aspects with Nottingham Grading System (NGS) of invasive breast carcinomas in a tertiary care center in Chattogram region in Bangladesh.

### MATERIALS AND METHODS

It was a cross-sectional descriptive study which was carried out in the Department of Pathology of Chittagong Medical College (CMC) Chattogram, Bangladesh. Study period was for one year from 1<sup>st</sup> April 2014 to 31<sup>st</sup> March 2015. After receiving excision/incision biopsy of breast tumor, specimens were meticulously examined, placed in a bottle containing 10% formalin for over night fixation. Tissue blocks were selected from the specimen, processed and sectioned to make slides, were stained by Haematoxylin & Eosin (H&E). The stained sections were examined in the light microscope to get a definite histological diagnosis of the lesions. Fifty (50) consecutive patients of invasive breast carcinomas of no special type were selected. Then histologically diagnosed invasive breast carcinomas (of no special type) were graded according to Nottingham Grading System (NGS)<sup>7</sup> (Table I). After taking written consent, a brief clinical history was taken from all fifty patient of histologically diagnosed invasive breast carcinoma. Special emphasis was given to record age, occupation, marital history, parity, and family history, history of breast feeding and use of contraceptives. Clinical examination findings were taken from the patient case record file. Finally, data was analyzed by computer using SPSS version 20 software.

### RESULTS

The age range of 50 patients was 24 to 75 years. The mean age was 46.52 years (SD  $\pm$  10.86) and the median age was 45 years. The patients were divided into six age groups. Majority of the patients i.e 18 (36%) belonged to the age group 41-50 years (Table II).

It was observed that the right breast was more commonly involved i.e in 31 (62%) patients, whereas left breast was affected in 19 (38%) patients. Upper and outer quadrant (38%) was the most common site followed by lower and outer quadrant (22%). Morphologically, 42 (84%) out of 50 patients had gross pathological tumor size ranging from 2 cm up to 5 cm, 04 (8%) patients had < 2 cm and remaining 04 (8%) patients had > 5 cm tumor size. Gross appearance of puckering was seen in 8 (16%) cases, peau d' orange in 7 (14%) cases, overlying skin ulceration in 4 (8%) cases and 31 (62%) lesions were either normal in appearance or they were received as incisional biopsy. Axillary lymph node involvement was seen in 19 (38%) cases and nodal metastasis was not seen in 31 (62%) patients (Table III).

Considering menopausal state, 22 (44%) patients were in pre-menopausal phase and 28 (56%) patients were in post-menopausal state. Among them, 26 (52%) patients had off spring ranging from 1 to 3 in number and 22 (44%) patients had offspring more than 3 in number. Majority of the patients i.e 35 (70%) patients were accustomed with use of contraceptives. Among them, 20 (40%) patients had a history of using oral pill, 09 (18%) patients took surgical contraception. Regarding family history, only 01 (02%) patient had family history of breast carcinoma and 02 (04%) patients had family history of malignancy in other site of the body.

Regarding Nottingham Grading System (NGS) 17 (34%) cases were grade I, 31 (62%) cases were grade II and 02 (04%) cases were grade III (Table IV, Figure 1, 2 & 3).

Regarding size of lesions in relation to histological grading out of 42 lesions with 02- 05 cm size, 14 (33.33%) lesions were grade I, 26 (61.9%) lesions were grade II and 02 (4.8%) lesions were grade III. Considering appearance of lesions, out of 31 lesions with no abnormality in appearance, 14 (45.2%) lesions were grade I and 17 (54.8%) lesions were grade II. Out of 07 lesions with peau d' orange, 71.4% (05) lesions were grade II and 14.2% (01) lesion was grade III. Among 08 lesions with puckered skin, 87.5% (07) lesions were grade II. Out of 19 cases with metastatic lymph node, 42.1% (08) cases were grade I, 52.6% (10) cases were grade II.

**Table I:** Nottingham Grading System (NGS).

Feature	Score 1	Score 2	Score 3
Tubule formation	>75%	10-75%	<10%
Nuclear pleomorphism	Small, regular uniform cells	Moderate variation in size/shape	Marked nuclear pleomorphism

Mitosis per 10 hpf\* in

44 mm field diameter	0-5	6-10	>=11
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Grade I : Score 3-5 well differentiated.

Grade II : Score 6-7 moderately differentiated.

Grade III : Score 8-9 poorly differentiated. \*hpf=high power field.

**Table II:** Descriptive statistics and distribution of age (n = 50).

Age in Groups (Years)	Frequency	Percentage (%)	MEAN (Years)	SD (Years)	MEDIAN (Years)	RANGE (Years)
21 – 30	03	06.0				
31 – 40	15	30.0				
41 – 50	18	36.0				
51 – 60	09	18.0	46.52	10.86	45.00	24 – 75
61 – 70	04	08.0				
71 – 80	01	02.0				
Total	50	100.0				

**Table III:** Distribution of lesion related variables (n = 50).

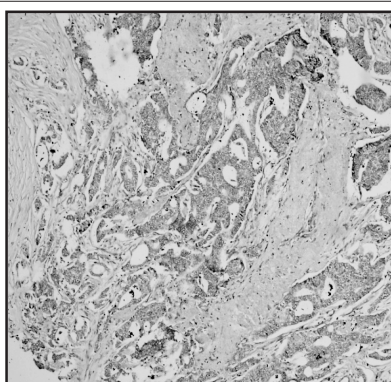
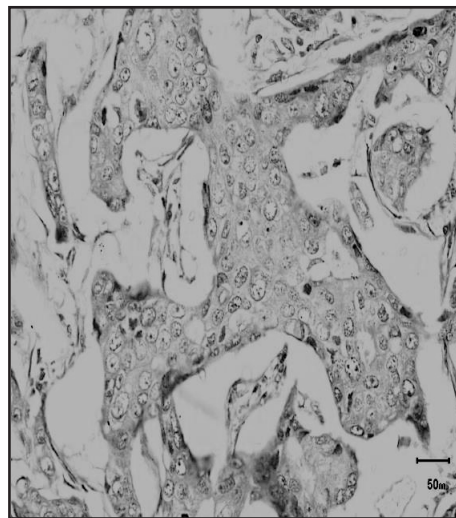
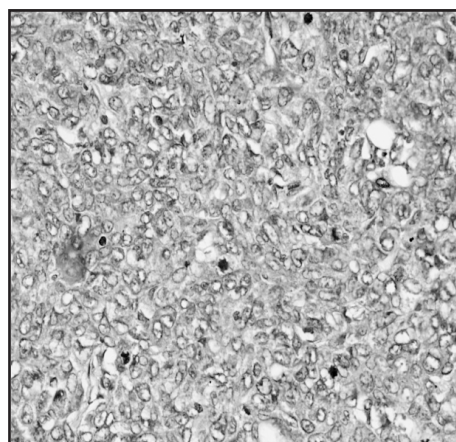
Variables Related with Lesion	Frequency	Percentage (%)
Side of Lesion		
Right	31	62.0
Left	19	38.0
Site of Lesion		
Upper & Outer	19	38.0
Upper & Inner	10	20.0
Lower & Outer	11	22.0
Lower & Inner	10	20.0
Size of Lesion		
> 5 cm	04	8.0
2 – 5 cm	42	84.0
< 2 cm	04	8.0
Appearance		
Normal	31	62.0
Ulceration	04	8.0
Peau d' orange	07	14.0
Puckering	08	16.0
Lymph Node		
Involved	19	38.0
Not Involved	31	62.0

**Table IV:** Distribution of Nottingham Grading System (NGS)(n = 50).

Grading	Frequency	Percentage (%)
Nottingham Grading System (NGS)		
Grade I	17	34.0
Grade II	31	62.0
Grade III	02	4.0
Total	50	100.0

**Table V:** Comparative table on distribution of cases- Nottingham Grading System (NGS).

Authors	MBR histological grading			Total No. (%)
	Grade I	Grade II	Grade III	
	No. (%)	No. (%)	No. (%)	
Rupom et al <sup>4</sup>	17(31.5%)	36(66.6%)	01(1.85%)	54(100%)
Pandsya and Shah <sup>7</sup>	25(42.37%)	24(40.68%)	10(16.95%)	59(100%)
Ravikumar and Rout <sup>17</sup>	22(22.4%)	56(57.14%)	20(20.4%)	98(100%)
Pandey et al <sup>14</sup>	07(23.33%)	19(63.33%)	04 (13.33%)	30(100%)
Phukan et al <sup>9</sup>	09(18 %)	28(56%)	13(26%)	50(100%)
Present study	17(34%)	31 (62%)	02 (04%)	50(100%)

**Figure 1 :** Invasive duct cell carcinoma, Grade-I Histopathology section (H & E stain) 400X.**Figure 2 :** Invasive duct cell carcinoma, Grade-II, Histopathology section (H & E stain) 400X.**Figure 3 :** Invasive duct cell carcinoma, Grade-III Histopathology section (H & E stain) 400X.

## DISCUSSION

The age range of 50 patients of this study was 24 to 75 years with a mean of 46.52 years (SD  $\pm$  10.86) and the median of 45 years. The age range was similar to the findings in Pakistan and India which were 25-75 and 25 to 83 years respectively<sup>8,9</sup>. Nisa et al showed median of their patient's age was 45.5 years and Bhargava et al reported mean age as 46.7 years, both were in accordance with findings of the present study<sup>8,10</sup>.

In present study, majority of the patients (36%) were in 41-50 years age. Phukan et al also reported maximum numbers of their patients were in 40–49 years age group<sup>9</sup>. Nisa et al and Sofi et al showed 66.0% and 59.1% of their patient's age at the time of diagnosis were  $\leq$ 50 years<sup>8,11</sup>. We found 72% patients were in that age which was a bit higher and may due to smaller sample size.



We found, 22 (44%) patients were in pre-menopause and 28 (56%) patients were in menopause. Though Gupta et al described 52% of patients in pre-menopause but Sofi et al observed that there is an increasing trend of occurring breast cancer in premenopausal women in India and Pakistan<sup>11, 12</sup>. As a part of Indian subcontinent, increased breast cancer incidence can be assume in pre-menopausal phase in Bangladesh and present study found a concordance with that observation.

Majority (60%) of the patients in present study did not use oral contraceptives. By analysis of a metaseres of combined 50 studies, Colditz and Chia showed that hormonal contraceptives had no significant role in developing breast cancer, which support the findings of the present series<sup>13</sup>.

This study found 62% of the lesions in the right breast which was in agreement with the findings of other studies as they found right breast involvement in 58.2% and 63.33% cases<sup>4,14</sup>. Upper and outer quadrant of the breast locates majority (38%) of the lesion in our study, though others reported higher percentage of 42.9% and 46.25% cases in that quadrant<sup>11,15</sup>. Proposed hypothesis of greater amount of breast tissue in upper and outer quadrant as reflected by higher incidence of malignancies in that quadrant by Lee was also supported by our findings<sup>16</sup>.

On Nottingham Grading System (NGS) we found 31 (62%) grade II malignancies which comprised the most as also reported by numbers of other studies<sup>4,9,14,17</sup>. Rajan and Pai criticized this distribution and stated it as one of the limitations of histological grading in which there is unequal distribution of patients among all the 3 grades with over 50% of patients in grade II and which may due to over lapping of grade II with grade I and III<sup>1</sup>.

Morphologically, majority (84%) cases of this study had gross pathological tumor size ranging from 2 cm up to 5 cm. Other studies had tumor size of 2-5 cm in most of their cases but with lower percentages<sup>11,17</sup>. But large tumor (>5 cm) is less frequent (08%) in present study which was in concordance with a Bangladeshi study as they showed 07 (2.78%) large sized tumor out of their 251 breast carcinoma cases<sup>3</sup>. It indicates early presentation in our set-up which may be due to consciousness and more easy access to the health facilities.

Regarding tumor size with histological grading, out of 04 small sized tumors, 02 (50%) tumors were grade I and 02 (50%) tumors were grade II. Out of 42 lesions with 02- 05 cm size, 14 (33.33%) lesions were grade I, 26 (61.9%) lesions were grade II and 02 (4.8%) lesions were grade III. Out of 04 large sized tumors, 01 (25%) tumor was grade I and 03 (75%) tumors were grade II. So higher grade of malignant tumor was seen with increasing tumor size in our study support Cioroboreanu and Lazar as they stated larger invasive breast carcinomas have a poorer outcome than those with smaller lesions<sup>18</sup>.

Regarding morphologic appearance with histological grading, out of 08 cases with puckering, 07 (87.5%) cases were grade II. Out of 07 cases with Peau d' orange, 05 (71.4%) lesions were grade II and 01 (14.2%) lesion was grade III. So all malignant lesion with abnormal appearances showed high grade tumors.

In present study, axillary lymph nodes were involved in 19 (38%) cases. Rakha et al observed lower incidence (24.4%) of lymph node metastasis in UK<sup>5</sup>. In UK, women are under regular mammographic screening and breast cancer cases are detected early and thus their lymph node involvement is low in comparison to our country.

Regarding axillary lymph node involvement with histological grading, grade I, II and III were found in 42.1%, 52.6% and 5.26% respectively in 19 cases with nodal metastasis. Again, 47.06% of all grade I cases, 32.26% of grade II cases and 50% grade III cases had nodal metastasis. Thus, in this study, lymph node metastasis was seen irrespective of the tumor grade. Ravikumar and Rout also couldn't establish association between tumor grading and incidence of lymph node metastasis<sup>17</sup>. However, different studies correlated tumor grading with lymph node involvement and found that higher grade tumors more likely to metastasize than low grade tumors. Dash et al studied 93 cases of invasive duct cell carcinoma and found that 74.2% of grade III carcinomas had nodal metastasis in contrast to 27% of grade I tumors<sup>19</sup>.

## CONCLUSION

Histologic grading provide an overview of the intrinsic biologic characteristics of the tumors. Our study also showed that patients with high grade tumors have some aggressive clinical and morphological presentations.

## RECOMMENDATION

We recommend routine assessment of histologic grade of breast cancer using the Nottingham Grading System (NGS).

## DISCLOSURE

All the authors declared no competing interest.

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