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## Original Article

# Clinico-pathological features of breast cancer: A Hospital-Based Case-control Study

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***ABSTRACT***

***Background:*** *Breast cancer is the most frequently diagnosed cancer in females. It has a major impact on health of women. According to a World Health Organization [WHO] estimate, more than 1.2 million people are diagnosed with breast cancer worldwide every year. The aim of the study was to evaluate the clinico-pathological features of breast cancer patient* ***Methodology:*** *This case control study was conducted in Department of Surgery, Sylhet MAG Osmani Medical College Hospital, Sylhet and Shaheed Shamsuddin Hospital, Sylhet during January 2012 to June 2012. Sixty-five women with breast cancer fulfilling the inclusion and exclusion criteria were taken in case group and age-stratified random sample of 65 women without breast cancer were taken in control group.* ***Results:*** *The mean age of the patients was 48.9 (SD ±8.7) years in case group and 47.8 (SD ±8.7) years in control group (p>0.05). Breast lump (96.9%) was the most common presentation. Tumour size was between 2.1 to 5 cm in 36 (55.4%) patients, tumour size was >5 cm in 27 (41.5%) patients and tumour size was <2 cm in 2 (3.1%) patients. Lymph node was positive in 17 (26.2%) cases and negative in 48 (73.8%) cases. The most of the cases 50 (76.9%) histological type of the tumour in this study were invasive ductal carcinoma and 9 (13.9%) were ductal carcinoma in situ and rest 6 (9.2%) were invasive lobular carcinoma. Grade-III constituted 30 (46.2%) cases, grade-II in 24 (36.9%) cases and grade-I in 11 (16.9%) cases. Stage-II constituted 27(41.6%) cases, stage-III in 21 (32.3%) cases, stage-IV in 11 (16.9%) cases and stage-I in 6 (9.2%) cases.* ***Conclusion:*** *Most of the patients in our country present with advanced stage of breast cancer, at which time there would metastasis leading to a low survival rate. Early detection and therapeutic advances have been made with considerable improvement in disease-free and overall survival in breast cancer.*

***Keywords:*** *Breast cancer, Clinical presentation, Histology, Staging*

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## INTRODUCTION

Breast cancer is by far the most frequent cancer of women (23% of all cancers),[1] and the third most common cancer overall, throughout the world.[2] The World Health Organization estimated breast cancer incidence is more than 1.2 million new cases per year in the world, accounting for 22% of the all newly diagnosed cancer cases. This corresponds to a lifetime risk for a woman of about 6.2% in developed countries (on average) and 2.2% in developing countries.[3] More than half of the cases are in industrialized countries - about 361,000 in Europe (27.3% of cancers in women) and 230,000 in North America (31.3%). Incidence rates are high in most of the developed areas (except for Japan, where it is third after colorectal and stomach cancers), with the highest age-standardized incidence in North America (99.4 per 100,000).[4] The incidence is more modest in Eastern Europe, South America, Southern Africa, and Western Asia, but it is still the most common cancer of women in these geographic regions. The rates are low (<30 per 100,000) in most of Africa (with the exception of South Africa) and in most of Asia. The lowest incidence is in Central Africa (ASR, 16.5 per 100,000).[1] In our subcontinent, breast cancer is the most frequent female cancer in Pakistan, accounting for almost 26.6%.[5] In Bangladesh, breast lesions particularly breast cancer are one of the common clinical problem. There is no exact data about the incidence of breast cancer in our country. In a study shows, it is the second most common cause, responsible 16.74% cancer death among the Bangladeshi female.[6]

Breast cancer presentation features do not alter much in the elderly. The most frequent sign of breast cancer is a painless lump. A new lump in an older woman is more likely to be cancerous. Breast pain, thickening, swelling, or nipple symptoms such as discharge or retraction should be vigorously pursued in older women. Infiltrating ductal carcinoma remains the most common histological subtype of breast cancer diagnosed in older and younger patients.[7] The majority of new patients with breast cancer present with Stage I or II disease: an observation that holds true for both young and old patients. In contrast, the most elderly cohort (age ≥85) are more likely to present with metastatic disease (approximately 9%) or an unknown stage at the time of study analysis.[7,8] Prognosis and management of breast cancer are influenced by classic variables such as histological type, tumour grade, tumour size, lymph node status, hormone receptor expression along with Her-2/neu status.[9] Advanced stage of presentation has remained a dilemma for the treating oncologists and surgeons in our country. Many NGOs, hospitals and clinics have been running programmed to increase awareness about this malignancy but currently there is no national population-based screening programme in Bangladesh. In this study we want to see the socio-demographic clinical and histopathological characteristics of breast cancer in its development in our perspective.

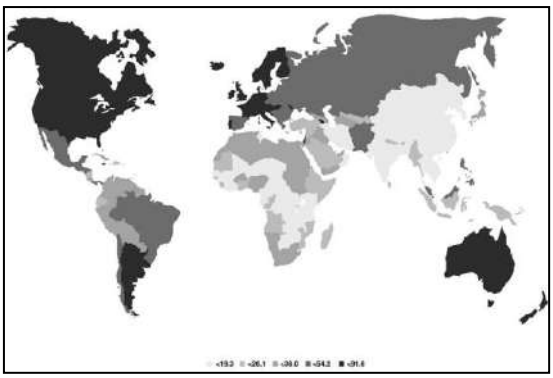

**Fig 1: Breast cancer incidence worldwide: age-standardized rates (world population) Geographic variation of Breast cancer.[10]**

## Materials and methods

This was a case-control study conducted in the department of Surgery, Sylhet M.A.G. Osmani Medical College Hospital, Sylhet and Shaheed Shamsuddin Hospital, Sylhet from January 2012 to June 2012. All female patients with primary carcinoma of breast irrespective of their age and who underwent breast surgery were included in the study. Carcinoma of male breast, patient with secondary breast carcinoma & patients those were not interested to participate in the study were excluded. In this study we took 65 women with breast cancer fulfilling the inclusion and exclusion criteria was taken in case group and age-stratified 65 women without breast cancer were taken in control group. Consecutive, convenient and exhaustive sampling was applied in selecting case group and age-stratified random sampling in selecting control group. Pre-designed data collection sheet designed for the study.

**Procedure of data collection:** Control subjects were selected from attendant accompanying the patients or other admitted patients without breast cancer in such a way that they were same age group. After maintaining privacy and in presence of female attendant details history was taken from all patient especially reproductive factor such as age at menarche, age at 1st pregnancy, parity, breast feeding and age at menopause. Examinations of the patients included general examinations with regard to built, anaemia, jaundice, lymphadenopathy, evidence of any acute infection. Local examination was done with thorough examination of the breast lump including the site, size, consistency, mobility of the breast lump, fixation with underlying structure and overlying skin and any ulceration of overlying skin, nipple retraction, peau d' orange; and also the axilla and contralateral breast. Systemic examination including respiratory, cardiovascular and central nervous system were also done.

Investigations were carried out for blood for TC, DC, ESR, Hb level, blood sugar, blood grouping, serum creatinine and relevant liver function test, X-Ray Chest P/A view, USG of abdomen, FNAC of the breast lump. Other relevant investigations for anaesthesia and operative fitness were also done. Per-operative findings were noted in selected cases where operative procedure was performed.

The specimen was preserved in 10% formalin and was sent to pathology laboratory for histopathology and histopathological grading. Histopathological grading was done by Bloom Richardson grading system as

grade 1, 2 and 3. Axillary sampling or clearance was carried out in all selected cases according to stage of carcinoma. All these lymph nodes were also preserved in 10% formalin and was sent to pathology laboratory for histopathology to assess the presence of metastasis. All the findings were recorded in the predesigned questionnaire.

**Statistical Analysis**: After collecting data editing was done manually and analyzed with the help of computer software program such as SPSS version 16.0 (Statistical package for social science). Quantitative data was analyzed by mean and standard deviation.

**Ethical consideration:** All the participants in the study were informed about the purpose of the study and written consent was taken before participation. All information was collected confidentially with complete respect to the patient wish and without any force or pressure. The protocol was approved by the Ethical Committee of Sylhet MAG Osmani Medical College, Sylhet.

## RESULTS

Table-I showed the distribution of the respondents by age. The age of the patients ranged from 31 to 69 years with the mean age of 48.9 (SD 8.7) years in group-A; whereas the age of the patients ranged from 31 to 68 years with the mean age of 47.8 (SD 8.7) years in group-B. The mean age of the patients in both groups was almost identical (Z=0.735; p>0.05). In group–A 26 (40.0%) patients were in the age group of 41 to 50 years, 22 (33.8%) patients were in the age group of 51 to 60 years, 9 (13.8%) patients were in the age group of 61 to 70 years and 8 (12.3%) patients were in the age group of 31 to 40 years; while in group-B it was 9 (13.8%), 27 (41.5%), 20 (30.8%) and 8 (12.3%) respectively. There was no statistically significant difference between the age group of the patients in group-A and group-B (p>0.05). In group-A, educational status was illiterate in 31 (47.7%), education below 10 years in 25 (38.5%) and 10 years or more in 9 (13.8%) cases. While in group-B educational status was illiterate in 35 (53.8%), education below 10 years in 23 (35.4%) and 10 years or more in 7 (10.8%) respondents. The difference between the two groups in relation to educational status was not statistically significant ($\chi^2$=0.576; p>0.05). The socioeconomic status of the patients was grouped into lower class, middle class and higher class. Socio-economic status was lower class in 39 (60.0%), middle class in 20 (30.8%) and upper class in 6 (9.2%) patients; while it was 34 (52.3%), 26 (40.0%) and 5 (7.7%) respectively in control group. The difference between the two groups in relation to socio-economic status was not statistically significant (p>0.05). The distribution of respondents according to their residential status was reported. In group-A, 45 (69.2%) patients were from rural area and 20 (30.8%) were from urban area. Whereas in group-B, 44 (67.7%) respondents were rural and 21 (32.3%) were urban by social background. The difference between the two groups in relation to social background was not statistically significant (p>0.05).

The distribution of major symptoms on admission was shown in table 2. Sixty-three (96.9%) patients presented with breast lump, 12 (18.5%) with bloody discharge from nipple, 5 (7.7%) patients with ulceration of overlying skin and/or nipple and areola; and 24 (36.9%) with weight loss.

Distribution of patients by major signs on admission was shown in table 3. Breast lump was present in all patients [(65 (100.0%)], retraction of nipple in 9 (13.8%), Deviation of nipple in 6 (9.2%), peau d'orange in 24 (36.9%), ulceration of overlying skin and/or nipple and areola in 5 (7.7%), fixation with overlying skin in 18 (27.7%), fixation with underlying muscle in 15 (23.1%), palpable axillary lump in 14 (21.5%) and satellite nodule in 2 (3.1%) cases.

Distribution of patients according to quadrant of breast involvement was shown in figure 1. Upper outer quadrant was involved in 38 (58.5%) patients, upper inner quadrant was involved in 13 (20%) patients, lower outer quadrant was involved in 11 (16.9%) patients, lower inner quadrant was involved in 1 (1.5%) patients and central breast was involved in 2 (3.1%) patients.

Table 4 showed distribution of respondents according to size of breast tumour. Tumour size was between 2.1 to 5 cm in 36 (55.4%) patients, tumour size was >5 cm in 27 (41.5%) patients and tumour size was <2 cm in 2 (3.1%) patients.

The most of the cases 50 (76.9%) histological type of the tumour was invasive ductal carcinoma and 9 (13.9%) cases were ductal carcinoma in situ and rest 6 (9.2%) were invasive lobular carcinoma. Distribution of respondents according to histological type was shown in figure 2.

Distribution of respondents according to lymph node involvement was shown in figure 3. Lymph node was positive in 17 (26.2%) cases and negative in 48 (73.8%) cases.

Regarding histological grading, grade-III constituted 30 (46.2%) cases, grade-II in 24 (36.9%) cases and grade-I in 11 (16.9%) cases. Distribution of respondents according to histological grading was shown in figure 4.

**Table 1: Socio-demographic characteristics of the respondents**

| Socio-demographic characteristics of the respondents | Group-A (n=65) | Group-B (n=65) | p value |
|---|---|---|---|
| **Age distribution** | | | |
| 31-40 years | 8 (12.3%) | 9 (13.8%) | |
| 41-50 years | 26 (40.0%) | 27 (41.5%) | |
| 51-60 years | 22 (33.8%) | 20 (30.8%) | |
| 61-70 years | 9 (13.8%) | 8 (12.3%) | |

| | | | |
|---|---|---|---|
| Mean (SD) years | 48.9 (SD 8.7) | 47.8 (SD 8.7) | p>0.05 |
| **Level of education** | | | |
| Illiterate | 31 (47.7%) | 35 (53.8%) | |
| <10 years | 25 (38.5%) | 23 (35.4%) | |
| ≥ 10 years | 9 (13.8%) | 7 (10.8%) | |
| Total | 65 (100%) | 65 (100%) | p>0.05 |
| **Socio-economic status** | | | |
| Lower class | 39 (60%) | 34 (52.3%) | |
| Middle class | 20 (30.8%) | 26 (40%) | |
| Higher class | 6 (9.2%) | 5 (7.7%) | |
| Total | 65 (100%) | 65 (100%) | p>0.05 |
| **Residential status** | | | |
| Rural | 45 (69.2%) | 44 (67.7%) | |
| Urban | 20 (30.8%) | 21 (32.3%) | |
| Total | 65 (100%) | 65 (100%) | p>0.05 |

SD= Standard deviation

**Table 2: Distribution of patients by major symptoms on admissio (n=65)**

| Major symptoms | Percentage |
|---|---|
| Breast lump | 96.9 |
| Nipple discharge | 18.5 |
| Ulceration of overlying skin and/or nipple and areola | 7.7 |
| Weight loss | 36.9 |

**Table 3: Distribution of patients by major signs on admission (n=65)**

| Major sign | Percentage |
|---|---|
| Breast lump | 100.0 |
| Retraction of nipple | 13.8 |
| Deviation of nipple | 9.2 |
| Peau d'orange | 36.9 |
| Ulceration of overlying skin and/or nipple areola | 7.7 |
| Fixation with overlying skin | 27.7 |
| Fixation with underlying muscle | 23.1 |
| Palpable axillary lump | 21.5 |
| Satellite nodule | 3.1 |

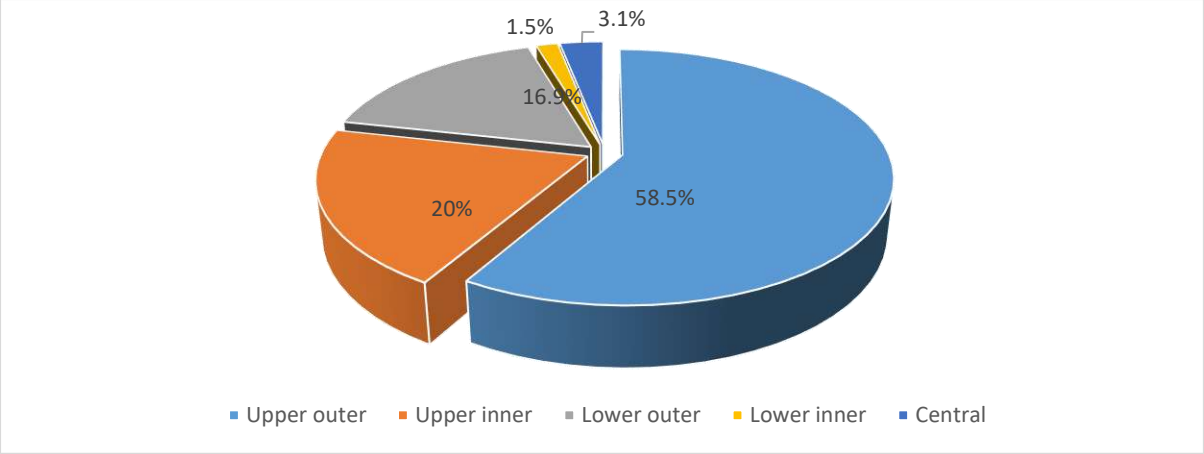


**Figure 1: Distribution of patients according to quadrant of breast involvement (n=65)**

**Table 4: Distribution of respondents according to size of breast tumour (n=65)**

| Size | N(%) |
|---|---|
| <2 cm | 2 (3.1%) |
| 2.1-5 cm | 36 (55.4%) |
| > 5 cm | 27 (41.5%) |
| Total | 100.0 |

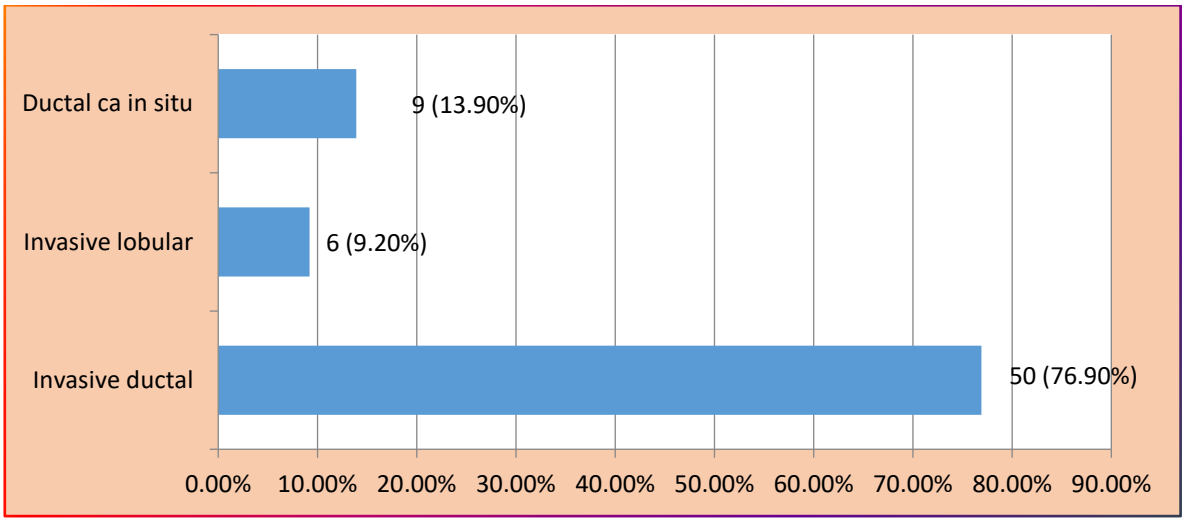


**Figure 2: Distribution of respondents according to histological type (n=65)**

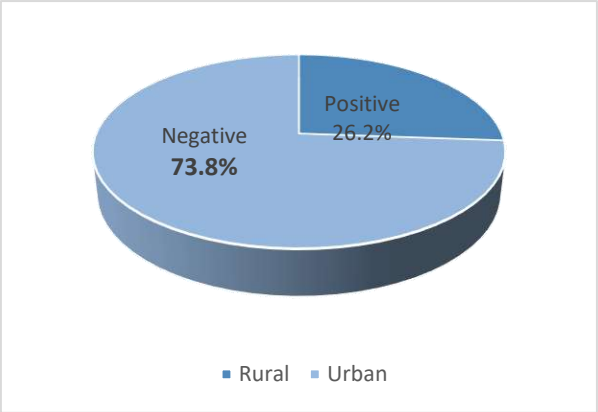


**Figure 3: Distribution of patients according to lymph node involvement (n=65)**

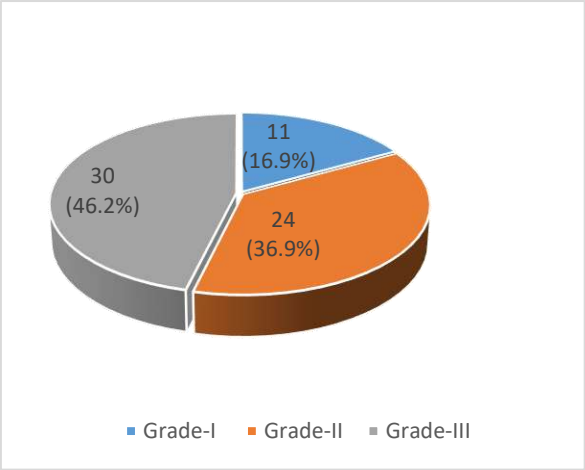


**Figure 4: Distribution of respondents according to histological grading (n=65)**

## DISCUSSION

From January to June 2012, the Department of Surgery at Sylhet MAG Osmani Medical College Hospital in Sylhet undertook a case-control research to analyze the clinicopathological aspects of breast cancer patients. In this study, the patients' ages varied from 30 to 69 years, with a mean age of 48.9 (SD 8.7) years in group A, and from 30 to 68 years in group B, with a mean age of 47.8 (SD 8.7) years. The mean age of the patients in both groups was almost identical (p>0.05). This result was similar to other studies.[9,11,12] Mamoon el al.[9] found the mean age of breast cancer was 48.0 ± 12 years; Gilani et al.[11] reported mean age of presentation of breast cancer was 47.5± 11.02 years and Malik,[12] found the mean age of breast cancer was 47.7 ± 11.8 years. This result was also supported by Wasserberg et al.[13] and Chan et al.[15] In their study Wasserberg et al.[13] found that the age of the patients was ranging from 31 to 71 years with the mean age of 53.1 (SD ±3.1) years and Chan et al. [9] observed the age of the patients was ranging from 29 to 84 years with the mean age of 53.7 years. In this regards Fleming et al.[15] found that age of the patients was ranging from 32 to 83 years with the median of 53 years. Ahlgren et al.[16] found that age of the women diagnosed as breast cancer between 40 and 74 years among their series. Aaltoma et al.[17] reported that

mean age at diagnosis of breast cancer was 59.4 (SD ±14.3) years.

This study also showed that 26 (40.0%) patients were in the age group of 40 to 50 years, 22 (33.8%) patients were in the age group of 50 to 60 years, 9 (13.8%) patients were in the age group of 60 to 70 years and 8 (12.3%) patients were in the age group of 30 to 40 years in group–A; while it was 9 (13.8%), 27 (41.5%), 20 (30.8%) and 8 (12.3%) respectively in group-B. There was no statistically significant difference between the age group of the patients in group-A and group-B ($p>0.05$). In this regard Colleoni et al.[18] found that 4.9% patients were below the age of 35 years, 39.0% patients were in the age group of 35 to 50 years, 30.4% patients were in the age group of 51 to 60 years and 25.7% patients were above the age of 60 years.

In the current study all patients (96.9%) presented with breast lump, 12 (18.5%) with bloody discharge from nipple, 5 (7.7%) patients with ulceration of overlying skin and/or nipple and areola; and 24 (36.9%) with weight loss; while the major signs were breast lump in all patients [(65 (100.0%)], retraction of nipple in 9 (13.8%), deviation of nipple in 6 (9.2%), peau d'orange in 24 (36.9%), ulceration of overlying skin and/or nipple and areola in 5 (7.7%), fixation with overlying skin in 18 (27.7%), fixation with underlying muscle 15 (23.1%), palpable axiilary lump in 14 (21.5%) and satellite nodule in 2 (3.1%) cases. These results were supported by other studies.[12] Malik,[12] found retraction of nipple (19.4%), discharge from nipple (6.9%), peau d'orange (8.4%), fixation with overlying skin (24.0%), fixation with underlying muscle (12.2%), palpable axillary lump (21.4%) and satellite nodule (4.2%) cases.

In the present study, left breast was involved in 36 (55.4%) patients and right breast was involved in 29 (44.6%) patients. This result was correlated with the study of Hye,[20] that left breast was involved in 57.7% and right breast was involved in 42.3% of female breast cancer patients. This result was also supported by Lester and Cotron,[19] that among the breast cancer patients left breast was involved in 52.4% of patients and right breast was involved in 47.8% of patients. Aftab,[21] found that the tumor were located 52% in the left side and 48% in the right side of breast. Naeem et al.[22] found 52.2% in left side and 47.8% in right side of their study patients

In this study upper outer quadrant was involved in 38 (58.5%) patients, upper inner quadrant was involved in 13 (20.0%) patients, lower outer quadrant was involved in 11 (16.9%) patients, lower inner quadrant was involved in 1 (1.5%) patients and central breast was involved in 2 (3.1%) patients. This result was correlated with Sainsbery,[23] that among the breast cancer patients upper outer quadrant was involved in 60.0% of patients, upper inner quadrant was involved in 12.0% of patients, lower outer quadrant was involved in 10.0% of patients, lower inner quadrant was involved in 6.0% of patients and central breast was involved in 12.0% of patients. Another study also supported this result of location of breast cancer was most common in upper outer quadrant (40.0%), 11% in the upper inner quadrant, 7% in the lower outer

quadrant, and 3% in the lower inner quadrant; 10.0% were centrally located and 25% overlapped quadrants; and 3.0% were multifocal.[24] In this regards Hye,[20] found the outstanding involvement of the upper outer quadrant was 38 (73.1%), followed by 7 (13.5%) in upper inner quadrant, 5 (9.6%) in lower outer quadrant and lowest involvement 2 (3.8%) in lower inner quadrant.

Regarding tumour size the present study showed that the tumour size was between 2.1 to 5 cm in 36 (55.4%) patients, tumour size was >5 cm in 27 (41.5%) patients and tumour size was <2 cm in 2 (3.1%) patients. This result was supported by Qaiyum,[25] that tumour size was between 2 to 5 cm in 37 (56.9%) patients, tumour size was>5 cm in 27 (41.5%) patients and tumour size was <2 cm in 1 (1.5%) patients. This result was differed from the study of Fleming et al.[15] that 30.0% of breast tumour was <2cm size, 61.0% were between 2-5cm size and 9.0% were >5cm size. In another study Kaur et al. [26] found that 24.3% of breast tumour were <2cm size, 56.1% were between 2-5cm size and 19.6% were >5cm size. Kakarala et al.[27] found in their studies that size variation of tumour as <1cm was 21.4%, 1-4 cm was 63.5% and >4 cm was 15.1%. Mamoon et al.[9] observed in their study that <2 cm was 18.8%, 2-5 cm was 50.6% and >5 cm was 30%. In our country females were hesitating to attend their physician about the breast lump due to shyness and religious background and lack of their health consciousness; and also there were no regular screening program for detection of breast cancer. So that they were lately presented and tumour size was larger in this study.

The most of the cases 50 (76.9%) histological type of the tumour in this study was invasive ductal carcinoma and 9 (13.9%) was ductal carcinoma in situ and rest 6 (9.2%) was invasive lobular carcinoma. This result was supported by Tan et al.[28] Fleming et al.[15] found that histological type of the tumour was invasive ductal carcinoma in 74.0%, invasive lobular carcinoma in 15.0% of cases and mixed type in 11.0% of cases. Tan et al.[28] found that 84.5% of cases the tumour was invasive ductal carcinoma and 3.2% of cases the tumour was invasive lobular carcinoma and 12.1% case other variety. Kuraparthy et al.[29] found 96.7% invasive ductal carcinoma, Mamoon et al.[9] reported 80.8% invasive ductal carcinoma and Naeem et al.[22] found 82% of breast cancer was invasive ductal carcinoma. All the above studies agreed with present study.

Regarding lymph node metastasis the present study showed that lymph node was positive in 17 (26.2%) cases and negative in 48 (73.8%) cases. This result was nearly correlated with the study of Laura et al.[30] that among their patients with breast cancer the axillary lymph node metastasis was found in 37.5% of cases and negative in 62.5% of cases. Social factor and lack of health consciousness of the patients in this region; and also there were no regular screening program for detection of breast cancer and thus they were lately presented and tumour size was larger as well as lymph node metastasis was more in this study.

Regarding histological grading, grade-III constituted 30 (46.2%) cases, grade-II in 24 (36.9%) cases and grade-I in 11 (16.9%) cases. Nearly similar result was observed by Tan et al.[28] found that 21.3% were grade-I tumour, 52.1% were grade-II tumour and 26.6% were grade-III tumour. In this regards Fleming et al.[15] found that 11.0% were grade-I tumour, 56.0% were grade-II tumour and 33.0% were grade-III tumour among their series. In another study Kaur et al.[26] found that 11.4% were grade-I tumour, 38.2% were grade-II tumour and 50.4% were grade-III tumour. Malik (2002) found that 12% Grade - I, 53% Grade - II and 35% Grade - III. Mamoon et al.[9] found in their study, 5.3% Grade - I, 64% Grade - II and 30.7% Grade - III. These variations occur due to geographical presentation, genetic involvement, sample size and also for study design.

## CONCLUSION

Late presentation with advance stage is the common feature of breast cancer patient in Bangladesh. It is easily understandable that the incidence and mortality of breast cancer is growing at a fast rate when it is extremely difficult to manage the deadly disease. Health seeking behavior is one of the important aspects of late presentation. Several studies showed that misconception and disbelieve is a significant factor for delayed health seeking behavior,[10] in Bangladesh where educational level is low and more than 40% people live below one dollar per day. More over government support is limited to delayed health seeking behavior is quite apparent. Because case-control nature, certain bias arises in the study. Case-control multi-centered study involving large sample size should be conducted to provide a better conclusion and recommendation. Taking oral contraceptives should be avoided and these women have other choices of contraceptives, such as barrier methods and intrauterine contraceptive devices. Women with risk of developing breast cancer should perform regular breast cancer screening, including monthly breast self- examinations, yearly clinical breast examinations and mammograms after the age of 40 years.

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