Original Article: Medical Sciences

BREAST CANCER: THE KYAMCH - CANCER CENTRE 7 YEARS EXPERIENCE

Corresponding Author: Dr. Md. Mofazzal Sharif, Associate Professor, Department of Radiology & Imaging, Khwaja Yunus Ali Medical Collage, Enayetpur, Sirajganj, Bangladesh.

Phone: +8801717017552, Email: mofazzal.sharif@gmail.com

Name and Designations of the authors:

1. Dr. Islam U. Chowdhury, PhD, Consultant Medical Oncologist, Ahsania Mission Cancer & General Hospital, Bangladesh.

2. Dr. Shahidul Islam, PhD, Associate professor, Department of Oncology, BSMMU, Bangladesh.

3. Dr. Md. Mofazzal Sharif, MD, MCPS, MPH, Associate Professor, Radiology and Imaging, KYAMCH, Bangladesh.

4. Dr. Md. Nayeem Ullah, MD, Assistant Professor & Head, Department of Radiology & Imaging, Monno Medical College Hospital, Bangladesh.

5. Prof. Dr. Md. Abdul Hai, FCPS, Director of Bangladesh Cancer Society, Bangladesh.

ABSTRACT

Introduction: Breast cancer is the most common cancer in women worldwide and also Bangladesh. It is a global problem causing significant mortality and morbidity.

In Bangladesh, it is the leading cause of cancer related death in female.

Objectives of the study: This current study is conducted with the objectives to describe sociodemographic characteristics of the

study subjects, histopathological, immunocytochemistry (IHC) reports and treatment status in terms of complete, incomplete treatment, drop out and death at Khwaja Yunus Ali Medical College and Hospital (KYAMCH).

Methodology: This observational descriptive study was conducted for seven years enrolling 623 subjects with breast cancer in Department of Oncology, KYAMCH.

Result: Majority of the subjects were female of reproductive age from 20 to 49 years age group having mostly invasive ductal cell carcinoma (72.87 %) with ER positivity (28.67 %) at IHC.

Conclusion: From this current study it was concluded that breast cancer awareness program should be strengthened as reproductive ages were mostly vulnerable and also to prevent incomplete treatment and dropout.

INTRODUCTION: Cancer is a growing health problem globally. Recently, about 10 million cases had been diagnosed with different kinds of cancer and the annual death rate is 6 million.[1] Breast cancer is a malignant tumor that starts in the cells of the breast tissue. This cancer is extremely heterogeneous disease with diverse morphology, different response to systemic therapy and variable clinical outcome. Worldwide breast cancer is the most frequently diagnosed life threatening cancer in women and leading cause of cancer death in women. But men can get breast cancer too. Not much information on breast cancer in Bangladesh is available. So far, effort made toward creating population-based cancer registries or a central cancer registry to provide comprehensive nationwide data has not been successful. Therefore, the

incidence and prevalence of breast cancer is mostly unknown. However, according to GLOBOCAN estimates based on the extrapolation of Indian data, 14,836 new breast cancer cases were diagnosed in 2012, with an age-standardized incidence rate (ASR) of 21.4 per 100,000.[1] This figure is likely to be an underestimate since many cases are missed due to lack of awareness, low level of education, misconceptions, poor socioeconomic status, insufficient access to health care, and poor governance. Picture may be similar in our country, 1st leading cancer in women is breast cancer (about 69%) which is related to significant mortality, morbidity in Bangladesh[2]. Incidence of breast cancer in Bangladesh is about 22.5/100000 in female and in case of Bangladeshi women, aged between 15-44 years, breast cancer has the highest prevalence 19.3 per 100000 compared to any other type of cancer.[3] However, under developing country like Bangladesh the

cancer management facilities are not evenly distributed the country. For this reason, most of the patients suffering from cancer are not getting appropriate treatment.[3-5] Over the last decades, our increasing understanding of natural course and cancer biology of breast cancer has led to revolute the management plan in this regard. Various methods and modalities are used now for diagnostic, prognostic and predictive factor evaluation. Surgery, chemotherapy, radiotherapy, hormone therapy and targeted therapy are available for the treatment of breast cancer. When and how these methods and modalities are to be rationally used for individual patient have paramount importance to achieve expected better outcome as shown in all available major breast cancer management protocols. In modern practice, examination and tests are done to find early cancer who do not have any symptoms. Aiming at reduction of morbidity and mortality and to offer a

dignified life.[5-9] However, under-developed country like Bangladesh the treatment situation is different. Most of patients come to health care delivery personnel when disease become advanced and serious. This is because of socio-economic condition, social stigma of the disease and fear of the cancer treatment.[10,11] This paper will cover the current perspective of breast cancer in Khwaja Yunus Ali Medical College and Hospital (KYAMCH) from 2011-2017, some issues for its' overall management and suggest a primary innovative strategy for the prevention of breast cancer that could be used for Bangladesh and other low-income countries like us.

METHODOLOGY: This observational descriptive was conducted at the Department of Oncology in collaboration with Department of Radiology & Imaging, KYAMCH for period of seven years from January 2011 to December 2017. Total 623 subjects with breast cancer were enrolled after obtaining informed written consent. Subjects who were initially diagnosed as a case of breast cancer were enrolled and followed up. Those subjects who were already diagnosed or underwent surgery were also enrolled. Data regarding age, gender, mode of surgery, histopathology type, immunohistochemistry (estrogen receptor, ER; progesterone receptor, PR and human epidermal growth factor receptor, HER2/neu) report, treatment status (in terms of completion, incomplete treatment, dropout, death) were collected. We analyzed these data in the Bangladeshi women and tried to determine their associations with patient's demographic age and clinicopathologic variables. Data was analyzed by SPSS V.20 and presented by bar, pie chart, and diagram.

RESULTS:

Table 1: Gender distribution of the study subjects (n=623)

Gender	N	%
Female	621	99.67
Male	02	00.33

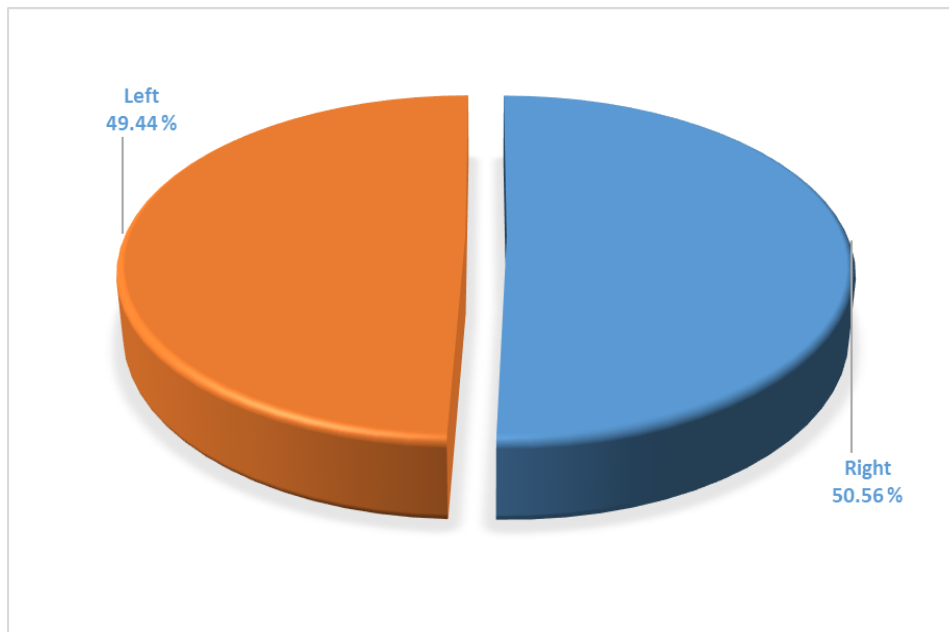Out of 623 study subjects, 621were female and 2 were male (Table 1).

Figure 1: Pie diagram showing side of involvement in study subjects (n=623)

Involvement of right side was seen in 315 (50.56 %) cases and left side in 308 (49.44%) (Figure 1).
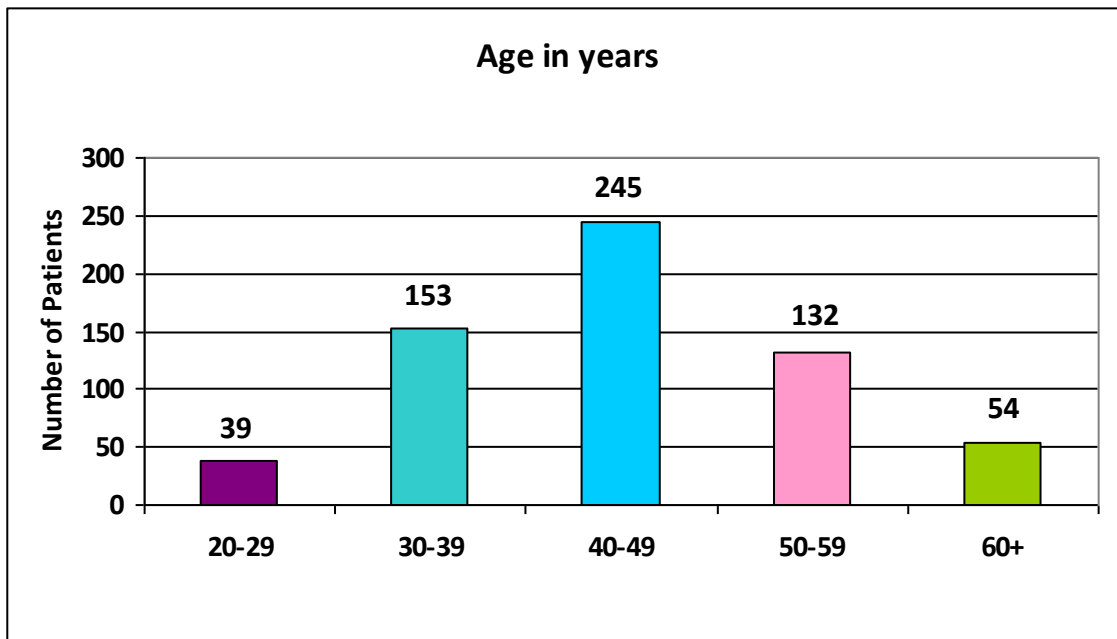

Figure 2: Age distribution of the study subjects (n=623)

Mean age of the study subjects was 43.56 (SD±12.87) years. Majority of the study subjects (39.23 %) were from 40 to 49 years age group. Only 8.66% subjects were above 51 years age group (Figure 2).

Table 2: Mode of surgery among study subjects (n=576)

Age group (Age in years)	N	%
Total mastectomy with axillary clearance	158	27.43
Simple mastectomy with axillary clearance	88	15.27
Excision of lump	83	14.40
MRM with axillary clearance	76	12.94
Simple mastectomy	52	09.32
Partial mastectomy	46	07.98
Radical mastectomy	35	06.07
Excision of axillary lump	29	05.03
Quadrantectomy	09	01.56

Among 623 study subjects, 47 subjects had undergone only FNAC. Rest 576 underwent surgery. Majority (27.43 %) was treated surgically by total mastectomy with axillary clearance method followed by simple mastectomy with axillary clearance (15.27 %), MRM with axillary clearance (12.94%) and only 1.56% underwent Quadrantectomy (Table 2).

Table 3: Histopathological subtype of breast cancer (n=623)

Histopathological subtype	N	%
Invasive ductal cell carcinoma	454	72.87
Infiltrative ductal cell carcinoma	148	23.77
Metastatic ductal cell carcinoma	11	01.76
Invasive papillary adenocarcinoma	02	0.32
Tubular carcinoma	02	0.32
Invasive mammary carcinoma	02	0.32
Intracystic papillary carcinoma	01	0.16
Metastatic mucin secreting adenocarcinoma	01	0.16
Medullary carcinoma	01	0.16
Lobular ductal cell carcinoma	01	0.16

Histopathological report revealed that majority of the subjects had Invasive ductal cell carcinoma [454 (72.87%)]. Infiltrative ductal cell carcinoma was prevailed in 23.77% cases and 1.76% subjects had Metastatic ductal cell carcinoma (Table 3).
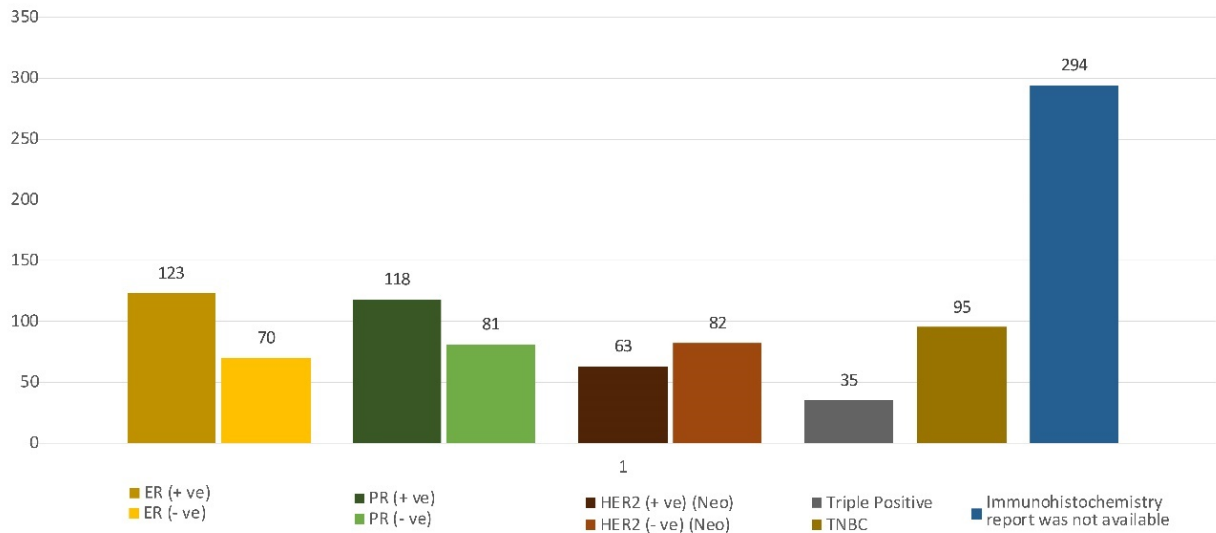
Figure 3: Immunohistochemistry of breast cancer (n=329) [Multiple responses were elicited].

Immunohistochemistry were done in 329 cases and it revealed that majority were ER positive (28.67%). PR positive cases were 27.5% and HER 2 negative were 24.92%. IHC report was not available in 294 subjects (Figure 3).
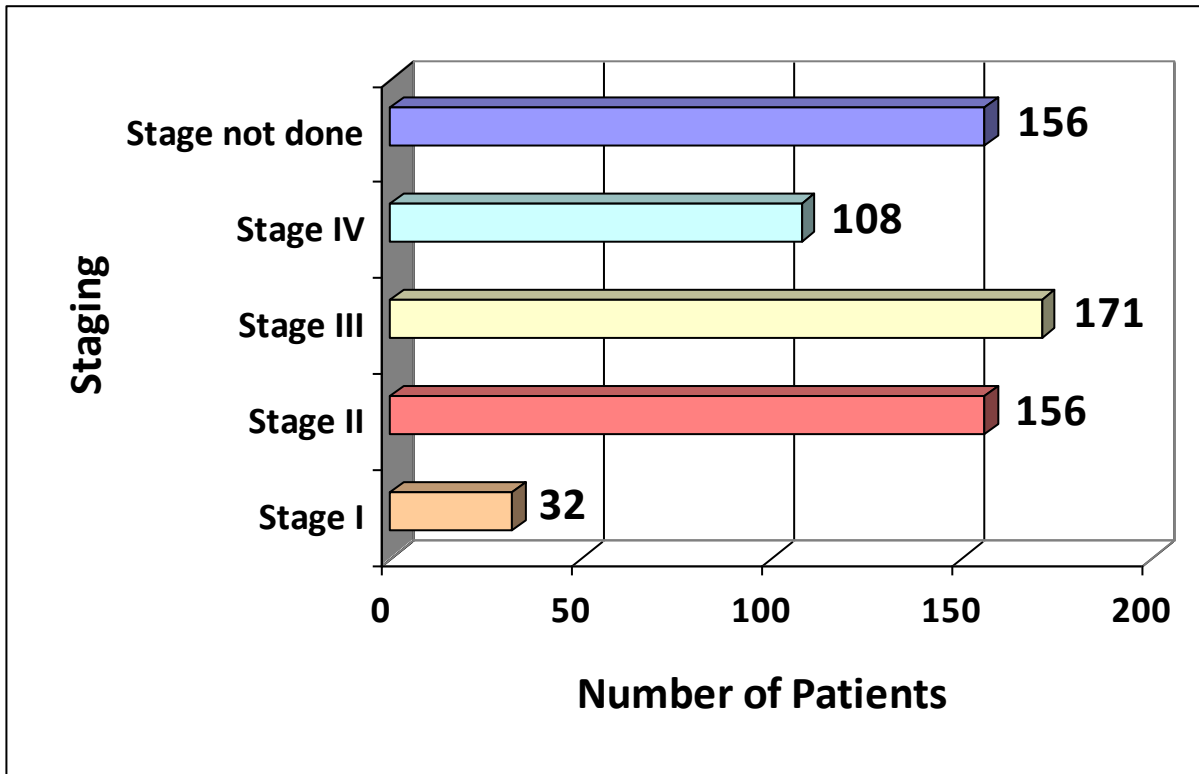
Figure 4: Group stage of breast cancer at time of presentation (n=623)

Staging was done in 467 subjects, majority were in stage III (36.61%). About 33.4% was in stage

II and 23.21% had distant metastases at stage IV. Staging was not done in 156 cases (Figure 4).
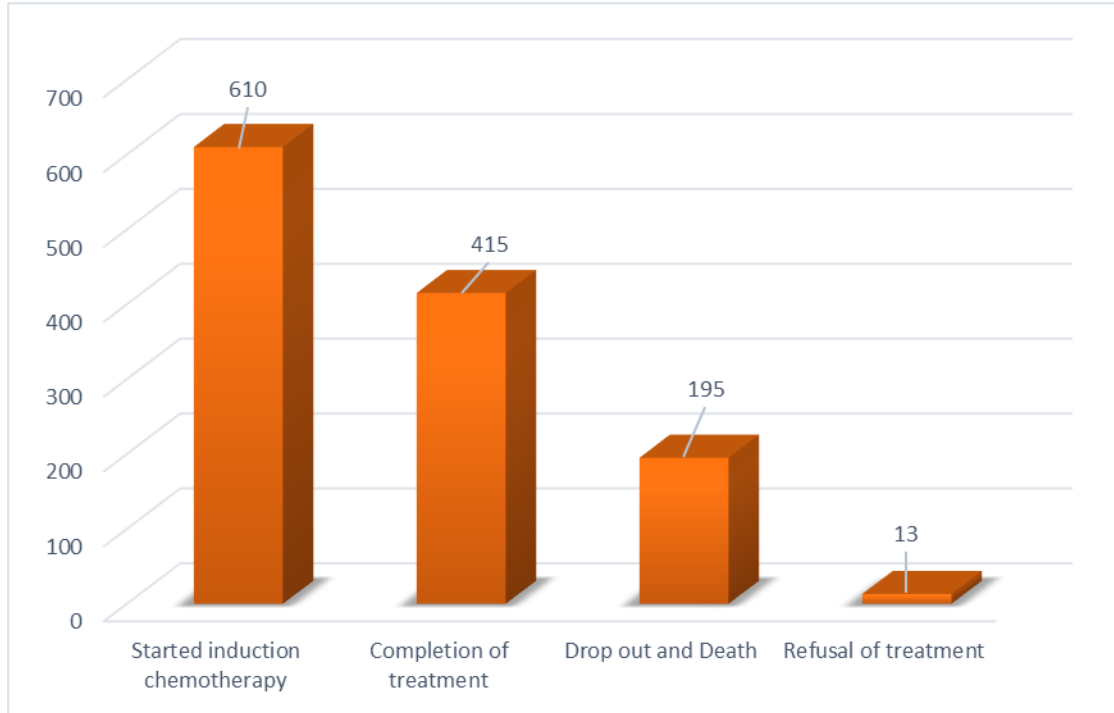
Figure 5: Profile of the patients at the end of seven years (n=610).

Among total patient, 610 received treatment and 13 patients refused treatment. At the end of seven years of observation, 415 subjects completed treatment, 186 patients were dropped out and nine patients were died (Figure 5).

DISCUSSION: With a population of over 163 million, Bangladesh is one of the most densely populated countries in the world.[12] Females have outnumbered males (84.1 versus 79.5 million) in the Bangladeshi population. About 45 million women are at reproductive age, while 13.5 million women are ≥50 years old.[13] As in other South Asian countries, the life expectancy of Bangladeshi women has increased significantly in recent years from 59 years in 1990 to 70 years in 2011.[14] Women are the key drivers of the Bangladesh economy and of its social transformation through their enormous contribution in the clothing industries[13] and in microcredit- and microfinance-based development programs.[15] Healthy women are vital for healthy families and communities. However, women's problems generally get a lower priority in Bangladeshi society. Although Bangladesh has made enormous progress in the healthcare sector especially related to infectious diseases, as recently highlighted by DeSantis[16]– the issue of cancer is given lower priority at both policy and research levels.[17]

The breast is a dynamic organ undergoes cyclical proliferative changes throughout life under the influence of hormones and growth factors, so may be likely to be more altered by environmental carcinogens.[12] Breast cancer remains a leading dreadful cancer of women worldwide. Even though the incidence of breast cancer in developing countries is lower that in their Western countries, it is rising rapidly. According to GLOBOCAN estimates, more than half (52.9%) of 1.67 million new breast cancer cases were diagnosed in developing countries in 2012[1], while the corresponding figure for 1980 was only 35%.[6] Although in developed countries breast cancer is mainly a disease of postmenopausal women (≥50 years), almost half of all breast cancer cases

(45%) in developing countries in 2010 were diagnosed in women of reproductive age (15–49 years).[6] For U.S. the cumulative lifetime risk for invasive breast cancer in women is 12%. In addition to sex, age is a major risk factor. The 10 year risks of invasive breast cancer at ages 40, 50, and 60 years are 1.5%, 2.3% and 3.5%, respectively. In 2016, about 250,000 U.S. women are estimated to develop breast cancer and 40,000 to die of it.[13] In Asia, the incidence of breast cancer peaks among premenopausal women in their forties; whereas among postmenopausal women in Western countries it peaks in their sixties.[7] The mortality of breast cancer is significantly higher in developing countries than in high-income countries. In 2012 nearly 62% of deaths associated with breast cancer occurred in developing countries.[1] Breast cancer is the most common cancer in women in Bangladesh. It has become a hidden burden which accounts 69% death of

women. In Bangladesh the rate of breast cancer occurrence is estimated to be 22.5 per 100000 females of all ages and in Bangladeshi women, aged between 15-44 years, breast cancer has the highest prevalence 19.3 per 100000 compared to any other types of cancer[3]. Cervical cancer causes in second for this group at 12.4 per 100000.[18-20] Since there is no national registry of cause of death in Bangladesh or of patients' follow-up systems in hospitals, it is not possible to know about the mortality and survivorship of breast cancer. Nonetheless, GLOBOCAN has estimated that 7142 women died of breast cancer in Bangladesh in 2012.[1] Apart from this, a maternal health survey estimated that cancer was responsible for 21% of all women's deaths in the reproductive age range.[21] Another verbal autopsy study showed that 62% of all deaths associated with breast cancer were in women under 50 years old.[22] Here a effort is made to do some work in

this direction. Healthy behaviors reduce breast cancer risk.[14] Physical activity of any type reduces breast cancer risk by about 12% in a dose-response effect. This benefit is unrelated to adiposity or menopausal status. Since postmenopausal obesity is linked to a higher risk of breast cancer, one might conclude that weight loss reduces risk, but this has not been studied directly.[15-17]

Table 4: Comparison of various aspects of Breast Cancer in KYAMCM Cancer Centre, (Bangladesh) & other countries (11, 12).

Features	KYAMCH (Bangladesh)	India	South Asian immigrant in UK/US	UK/US
Incidence (ASR per 100,000)	21.4*	25.8	40.5 vs 57.4	95 in UK and 92.9 in US
Mean Age (in years)	45.5	45 - 49	51.8	62.8
Premenopausal	70.14%	50%	45%	24.5%
ER (+ ve)	28.67%	52 - 60%	59 - 71%	70 - 79%
TNBC	29.91%	20 - 22%	19%	8 - 12%
Histology: Invasive ductal carcinoma	72.87%	88.5%	69.1%	65.6%
Initial Stage of diagnosis	III - IV: 29.91%	III - IV: 60%	III - IV: 16%	III - IV: 11%

* This finding was represented from the study by Parkin et al[1].

None of the breast cancer cases is detected by organized screening in Bangladesh, even though currently some scattered effort after are going on. Breast cancer can be detected at earlier stages by simple self-examination of the breasts[23], but most of the patients (more than 90%) seek medical attention at advanced stages: i.e., stages III and IV.[24,25] This scenario can similarly be seen in many resource-limited countries like India.[26] In Bangladesh, general health education is poor, and few people are aware of cancer.

Literature searches yielded only two reports on breast cancer knowledge and awareness among urban people of Dhaka city. In present study, most of the patients presented at stage II, III. One study conducted on 175 women of reproductive age showed that 41% of the participants had not even heard of breast cancer. About 94% of them mentioned that breast cancer is not a disease of old age.[27] This perception might have been acquired from the fact that the majority of the breast cancer cases in Bangladesh occur at a relatively young (premenopausal) age. Most of the respondents (about 77%) were unaware of breast cancer screening methods and more than 96% of them were unfamiliar with breast self-examination.[27] It is encouraging, however, that nearly 92% of the women interviewed would not hesitate to seek medical help from a physician when there are problems associated with their breast.[28] Another survey – conducted mostly on educated (65% > 12 years of school)

women, with 50% representing faculty members of a university – has shown that higher education is positively correlated with breast cancer screening practices and awareness.[29] Moreover, other factors – including the high cost of treatment, fear of social stigmatization, inadequate diagnostic facilities, and lack of trust in existing healthcare systems – might be barriers to women's decisions to seek medical help. For women with hereditary breast cancer mutations, prophylactic bilateral mastectomy is an effective alternative to chemoprophylaxis.[15] Breast cancer is different between develop countries and 3rd world countries where mainly postmenopausal women of more than 50 years are affected, but in developing countries, as mentioned earlier, breast cancer was diagnosed more in premenopausal women.[3,6-8] Present study result was similar with that findings. Mean age of the study subjects was 43.56

(SD±12.87) years. Majority of the study subjects (39.23 %) were from 40 to 49 years age group. According to an National Institute of Cancer Research and Hospital (NICRH) report, 5255 breast cancer cases were diagnosed during the period 2005-2010 of which 56% of the cases were women of reproductive age ranging from 15 to 44 years.[2] The mortality of breast cancer significantly higher in developing countries than in high income countries.[9] Not much information on breast cancer in Bangladesh is available, GLOBOCAN has estimated that 7142 women died on breast cancer in Bangladesh on 2012.[5] Success of treatment of breast cancer depends on IHC report. In Bangladesh, a retrospective study on 1042 cases demonstrated that 69% and 73% of the cases were ER- and PR-positive, respectively. About 28% of 335 cases showed Her-2/neu overexpression. Only 9% of patients had triple negative breast cancer (TNBC).[30] There was a strong correlation between ER and PR status, whereas the expression of Her-2/neu had an inverse relationship with hormonal receptor status. Approximately 40% of grade III tumors were ER/PR-positive.[30] Present study shows that IHC were done in 329 cases and it revealed that majority were ER positive (28.67%). PR positive cases were 27.5% and HER 2 negative were 24.92%. IHC report was not available in 294 subjects. The cause is possible due to, financial constrain of the patient as a lot of money was already spent during operation and biopsy. From all these seven years majority of patients came with stage II and III disease. Only 6.65% subjects were from stage I. This is possibly due to lack of knowledge of the patients or ignorance about breast cancer. In KYAMCH Cancer Center, among 623 breast cancer patients, 610 received treatment. During treatment course, 13 patients refused treatment. At the end of seven years of observation, 415 subjects completed

treatment, 195 patients dropped out and 9 of them died. Bangladesh, burdened with a huge population, is facing a severe shortage of human resources for health. There are approximately five physicians and two nurses available for every 10,000 people.[31,32] No national health insurance system exists in Bangladesh.[33] While over 70% of the population live in rural areas[34], most of the secondary and tertiary healthcare facilities are centered in urban areas, with exception of KYAMCH. Public hospitals are generally overcrowded and lack basic resources, including equipment and essential drugs. In contrast, private clinics and hospitals, like KYAMCH, are relatively well equipped, but these are financial constrain for most Bangladeshis.

However, this incident rate is growing up day to day due to unawareness of the people, lack of confidence about medical treatment, improper screening, maltreatment and lack of motivation to go for institutional

treatment and management. Furthermore, because of poor socio-economic infrastructure and atmosphere which loom large for the social stigma and instilment of fear among the patient, they keep themselves aloof from taking treatment of the patient with cancer. NICRH, Bangladesh has demonstrated a steady increase of breast cancer incidence. In Bangladesh, maternal mortality survey (2010)[35] cited that breast cancer was responsible for 21% of death of women between 15-49 years of age. Now a day, it is also a Public Health Concern. The official fight against cancer in Bangladesh can be attributed to the founding of the NICRH. A study[28] in Bangladesh showed that 87% of new cases of breast cancer stage III+, where cancer had spread to other regions and were incurable. The treatment options were rare, hopelessly very expensive and especially country with low resources such as Bangladesh. It has found the majority of the blame is on lack of public

awareness for detection. This is inevitably true in the rural areas of Bangladesh. Integrated health policy is needed with qualified and specialized oncologist, as they play a focal role in management of cancer patients. To avoid poor dealing with patients and reduce unwanted and unavoidable death, a crash program must be taken and run to create efficient and caring oncologist.

CONCLUSION: In current study it was observed that female as well as male were affected by breast cancer. Female of reproductive age were mostly affected. Although IHC plays important role in management of breast cancer, in current study one third of the patient had no IHC report. Also a large number patients were incompletely treated, some dropped out. So, breast cancer awareness program should be strengthened in more centers to overcome these problems.

Conflict of interest: None.

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