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Original Research Article

Spectrum of breast cancer patients: twin institutional study

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ABSTRACT

Background: Breast cancer is emerging as one of the most common cancer occurring in urban female population of India. It has become the second most common cancer in rural India, after cancer of uterine cervix. One must understand the diversity of presentation of breast cancer patients in the rural and urban population. Author is a surgeon working in a hospital which caters health care to both, rural as well as urban population. The present study is meant to review the data of various types of presentation, of cancer breast in two Institutes in different states. We also would like to compare our data with a few major cancer centers in metropolitan cities. The aim of the study was to present a data of patients with breast cancer at two institutes.
Methods: This is a retrospective observational study carried out at two different medical teaching Institutes, CCM Medical College, Kachandur, Durg, Chhattisgarh and other at NKP Salve Institute of Medical Sciences Nagpur, Maharashtra. Study was carried out from 2009 till 2016 and total of 167 patients were included in the study. Data like age, menstrual status, size of lump, stage of disease, grade of disease (Bloom Richardson Elliston Index) and ER, PR, HER/neu receptor status of tumor, presence or absence of metastasis, and follow up records related to outcome, are presented in this study.
Results: Out of 167 patients included in the study, two patients were males, and were excluded from our study. It becomes a study of 165 patients. Average age of patients at presentation was between 35 to 65 years. Majority of patients belong to stage III a (bulky operable disease) or III b, (locally advanced breast cancer) Stage II, and stage IV - metastatic disease. No patient of stage I disease reported in the present study. Most common pathological type was infiltrating ductal carcinoma.
Conclusions: Breast cancer has emerged as the commonest cancer in urban India, with second most common cancer in rural India. Majority of our patients present with advanced disease stage with numerous poor prognostic factors such as young age, larger tumor size, lymph node metastasis, high pathological grade and poor hormone receptor status. These factors are a reflection of poor health awareness for breast cancer, general indifference towards women's health, poor financial resources, unavailability of multimodality treatment facilities.

Keywords: Breast cancer, Grade, Outcome, Stage

INTRODUCTION

Indian subcontinent is known for wide ethnic, cultural, religious, economic diversity so also variation in the health care infrastructure. Pattern of healthcare facility is heterogeneous. There are regions where the benefits of awareness, early diagnosis and multidisciplinary treatment have not reached. With rising incidence and awareness, breast cancer is the commonest cancer in urban Indian females. It is 2nd most common cancer in rural population.[1] Myths and ignorance which prevails in our society result in an unrealistic fear about the disease.[2]

Urban population is getting the benefit of awareness programs but such programs have not reached the remote rural areas of the country.[2,3] Majority of our patients are presenting either in stage of Bulky disease or locally advanced breast cancer or metastatic stage.[2,4] One of the very predominant reasons found for this late presentation is negligence because of general indifference towards female health, in our society, but other factors like lack of screening programs, paucity of diagnostic aids. Other vital point of importance is, there are very few centers where the multidisciplinary treatment is available. This study aims at providing spectrum of presentation of breast cancer at two teaching institutes in two different states of India. While we present our data, we would be giving the overview of breast cancer scenario from some major cancer registries in India, Like SGPGIMS Lucknow, TMH Mumbai.

METHODS

This retrospective observational study was carried out at two collaborative teaching institutes and hospital, catering health care services to patients from rural and urban area, from September 2009 to March 2017. This study retrospectively compared the demographic, clinical, pathological and outcome data in breast cancer patients managed at these two teaching institutes.

Out of all patients of diagnosed breast cancer, we included those 167 patients where we can retrieve the complete data from available records. Two patients were male breast cancer and so excluded from study. Thus, it is a study in 165 patients. The related data was entered in prestructured proforma. It includes age, menstrual status, obstetric history, family history, clinical stage (TNM Stage), pathological type, histological grade, (Bloom Richardson Eliston Index), ER, PR, HER/neu status, presence or absence of metastasis. All these patients were followed, with standard follow up protocol, (once in every 6 months for 2 years, then every year for 3 years with clinical examination, X-ray chest, CT scan chest and ultrasound of abdomen, bone scan or other imaging if the patient is symptomatic) for a period from 1- 3- 5 years for assessment of status of loco regional disease and distant metastasis. Patients after confirmation of diagnosis of cancer breast, who are willing to participate in the study were enrolled. Standard protocol for metastatic work up was followed. Routine blood investigations, Liver function, Renal function, X-ray chest, CT scan of chest, ultrasonography of abdomen and pelvis was done in all patients. Patients in clinical stage III, IV or symptomatic for suspected metastasis were further subjected to isotope bone scan to rule out bone metastasis, and CT scan of brain. All patients who need surgery were treated with either standard Modified Radical Mastectomy, or breast conservation surgery, with adjuvant chemotherapy, and or radiotherapy wherever advised. Locally advanced breast cancer patients were treated with neoadjuvant chemotherapy, followed by surgery for residual disease in selected patients. Estrogen receptor positive patients were given Tamoxifen/ Aromatase inhibitors started at the end of chemotherapy and continued for 5 years.

Figure 1: Bulky operable disease stage iii a, retracted nipple in cancer breast, local recurrence after lumpectomy.

Figure 2: Surgery bilateral mastectomy in synchronous cancer of breast, familial disease.

Figure 3: Fungating mass-negligence-general indifference in healthcare towards females.

RESULTS

Present study includes 165 patients, with diagnosis of breast cancer, the commonest age of presentation is between 35 years to 60 years with youngest being 35 and oldest is 80 years. In our study, around 51 (31.27 %) patients were between the ages of 35 to 45 years. 114

(63.72 %) were between ages of 45-80 years. Average age at presentation is between 45-60 years. Breast cancer in Indian scenario is seen at comparatively younger age than in the western world. Where the common age is around 55-70 years.

Table 1: Age at presentation.

Age in years	No. of patients
35-45	51 (31.27 %)
46-65	103 (62.42 %)
66-80	11 (6.7 %)

As per the reports tumor size in breast cancer is important predictor of outcome of disease. The tumor size was ranging from 4.5 cm smallest to 10-12 cm largest. There was no patient with size of tumor less than 2 cm. Tumor size of 4.5 to 5 cm was present in 52 Patients (31.51%). Patients with tumor size more than 5 cm; 113 (68.49%) We had 27 patients (16.36%) presented with distant metastasis at the time of Initial diagnosis. Majority of patients belong to either III a, or III b (LABC) and no patients presented in stage I disease.

Table 2: Size of tumor.

Size of tumor	No. of patients
< 2.5 cm	Nil
Between 2.5 to 5 cm	52 (31.52 %)
Size more than 5 cm including LABC	113 (68.48%) LABC-44 (26.66) 42 (25.45 %) patients with bulky operable breast cancer.

Commonest histo-morphological type was invasive ductal cancer in 148 (89.69 %), invasive lobular cancer was seen in 11 (6.66 %), ductal carcinoma in situ; 3 (1.81 %) and medullary carcinoma was seen in 3 (1.81 %) patients.

Table 3: Histological types.

Histopathological type	Number of patients
Infiltrating duct carcinoma	148 (89.69 %)
Infiltrating lobular carcinoma	11 (6.66 %)
Ductal carcinoma in situ	3 (1.81 %)
Medullary carcinoma	3 (1.81 %)

In the present study only 97 patients of breast cancer were willing for receptor study from tumor. Only 36 (37.11 %) ER PR positive; considerably low level of receptor positivity than in western countries.[12] Triple negative patients 17 (17.52 %), 44 (45%) ER, PR negative.

In this series no patient underwent breast conservation surgery, Modified Radical Mastectomy (MRM) was done in 94 (57 %). Lymph node involvement was seen in 61 (63%) patients.

Table 4: Receptor study in 97 patients.

ER, PR positive	ER, PR negative	HER/neu	Triple negative
36 (37.11 %)	44 (45%) ER, PR negative	17 (17.52 %)	17 (17.52 %)

Table 5: Menstrual status of our patients.

Menstrual status	No. of Patients
Premenopausal	57 (34.54 %)
Post-menopausal	108 (65.46 %)

In the present study 57 (34.54 %) patients were premenopausal and 108 (65.46 %) belong to postmenopausal status.

Table 6: Tumor grade (Nottingham grading system).

Bloom Richardson Score	Differentiation grade	No. of patients
3,4,5	Well differentiated low grade	94
6,7	Moderately differentiated intermediate grade	32
8,9	Poorly differentiated high grade	39

Assessment of histological grade is an important determinant of breast cancer prognostication. Nottingham Grading System provides a simple, inexpensive, and highly accurate method for assessing tumor biological characteristics and patient prognosis. In the present study Nottingham Grading System [NGS] 94 (56%) belong to low grade, 32 (19.3 %) Intermediate grade, and 39 (23.63 %) high tumor grade.

In this study, we had two patients with operable synchronous breast cancer, where bilateral MRM was done followed by breast reconstruction after 1 year in one patient. Palliative chemotherapy, with or without hormonal therapy was offered to 27 patients with distant metastasis. Monoclonal antibody in the form of Herceptin in HER2/neu was afforded by only one patient. Survival statistics was recorded at the end of 1, 3, 5 years. In the present study, all patients presented with distant metastasis during initial presentation died within 2 years of diagnosis. In present study, 1-year survival was 90 %, 3-year Survival was about 74 %, 5-year survival was 58%. Most of the distant metastasis occurred within 3 years after treatment. The commonest site for distant Metastasis; bones, lungs, liver, and brain.

DISCUSSION

Breast cancer is the commonest cancer in women worldwide with a widely variable incidence between countries and regions.[1] Scenario in India; over 100000 new breast cancer patients are estimated to be diagnosed annually.[1,2,5,6] As per the ICMR data, breast cancer is the commonest cancer in urban women population. Registries of Delhi, Mumbai, Ahmedabad, Calcutta, and Trivandrum constitutes >30% of all cancers in female.[3,6] Rural area PBCR of Barshi, breast cancer is the second most common cancer after cancer of uterine cervix.[4,6] It is expected that in the coming decades, India would see a rise of incidence by 0.5-2% per annum[4]. A significant proportion of Indian breast cancer patients are younger than 35 years of age. This proportion varies between 11% at Tata Memorial Hospital, Mumbai (Dinshaw) to 26% at SGPGIMS. In the present study, around 51 (31.27%) patients were between the ages of 35 to 45 years.[10] 114 (69.09%) patients were between 45-80 years of age. Young age has been associated with larger tumor size, higher number of metastatic lymph nodes, poorer tumor grade, low rates of hormone receptor-positive status.[1,2,5,6] 154 (93.33%) of our patients are younger than 65 years. Marriage at an early age, early and multiple childbirths, breast feeding of all children for long period of time is the norm in most Indian societies. But urban female population is moving away from this trend, with late age childbirth, little or no breast feeding due to different social values and the demands of jobs on working women. In the present study 51 (31.27 %)of patients belong to the age group between 35-45 years. 5 (3.03 %) Nulliparous, positive hereditary history in 3 (1.81 %) of breast cancer. At SGPGIMS Lucknow, only about 5% of all patients had family history of breast/ ovarian cancer in first degree relatives. We did not have the facility for genetic screening BRCA 1, BRCA 2. All our breast cancer patients, self-detect their disease at the stage when it presents with a palpable lump or when it has given rise to secondary changes like local skin (invasion, ulceration, fungation), chest wall changes or distant metastasis.[7] The disease is seen outside the ipsilateral axilla in 6-25 % cases.[8] Many factors are responsible for this delayed presentation which includes lack of awareness about the disease, non-availability of health care screening programs for these patients, substantial postponement of visit to doctor even after detection of lump, lack of diagnostic facilities. Clinical staging is the important predictor of outcome, almost 44 (26.66%) of our patients were in a stage of locally advanced disease (IIIb) 52 patients (31%) of our patients were in stage II, not a single patient presented with stage I disease; 42 (41.83%) patients presented with operable bulky disease. In our series of 165 patients 27 (16.36 %) presented with distant metastasis. Registries from 4 major cancer centers in India suggest 50% patients present with locally advanced disease. Majority patients present with stage IIIb (SGPGI Lucknow -35%) and stage IIIa (27%).[9] Some 8-10 % of patients have TNM stage IV at the presentation. Only very few (approximately 5%) have stage I. Axillary lymph node metastasis is present in > 60 % of our patients with operable disease (T2, T3). The histopathological types seen in breast cancer patients indicates that invasive ductal carcinoma not otherwise specified (IDC NOS) was found to be the most common type. In present study 148 out of 165 patients had (IDC NOS) (89.69%) followed by infiltrating lobular carcinoma 11 (6.66%), ductal carcinoma in situ; 3 (1.81%), medullary carcinoma was seen in 3 (1.81%) patients. In study from New Delhi and SGPGIS Lucknow reports invasive ductal cancer (NOS) 88%, infiltrating lobular carcinoma; 3.7%, medullary cancer; 1.1%, (DCIS) is seen 1.1%, metaplastic types (0.9%) TMH Mumbai have 70% patients reported as having grade III or grade II disease.[10] The average tumor size in our patients is between 4.5-5.4 cm to 8-10 cm. Indian cancer registries quote the same average size.[11] In the present study receptor status was known only in 97 (58.78%) patients out of 165. Only 36 (37.11%) ER PR positive, considerably low level of receptor positivity than in western countries.[12] Triple negative patients were 17 (17.52%), 44 (45%) ER, PR negative. At TMH Mumbai, the ER + status was found in 33% and PR+ in 46% of patients.[13] A few reports say the low ER+ and PR+ in our patients may be because improper immunostaining techniques used. A study from major hospital from Mumbai reported that the ER-/PR+ reported on IHC were actually due to suboptimal manual assays, and when same tumors were evaluated using well standardized international kits they were found ER+, PR+.[14] HER2/neu another clinically useful variable was found positive in 17 (17.52 %) patients in the present study. According to Data from SGPGI Lucknow 20% Indian patients found positive for HER2/neu.[9] In all operable patients modified radical mastectomy was done with complete axillary clearance. Patients with LABC were treated with neo adjuvant chemotherapy + hormonal therapy in receptor positive patients, followed by surgery in about 47% of our patients. Palliative chemotherapy as advised by medical oncologist was offered to patients with distant metastasis. In the present series, all patients presented with distant metastasis died within 2 years of diagnosis. 1-year survival was 90 %, 3-year survival was about 74%, 5-year survival was almost 58%. Most of the distant metastasis occurred within 3 years after primary treatment. This is comparable to overall 5-year survival rate in the Bangalore PBCR has been reported at 42.3 %.[15] Chennai metropolitan tumor registry reported survival rates of 80%, 58% and 48% at 1, 3 and 5 years, respectively.[16] At SGPGIMS Lucknow, the 5-year overall survival rate was 62%. The 5-year actuarial survival has been 90% for stage I, 78 % for Stage II, 57 % for stage III, 22% for stage IV.[16] Breast conservation Surgery (BCS) is still offered to a miniscule proportion of patients.[10] In the present series out of 165 Patients not a single patient underwent (BCS) this is the reflection of late stage of the disease and unavailability of optimal facilities for radiotherapy, pathology and problem of follow up. Also there is low acceptance on the part of patients.[10] A study from New Delhi showed only 11.3%

underwent BCS, while MRM was performed in 88.7 % of patients.[12] The Breast unit at TMH Mumbai reports that the proportion of cases undergoing BCS has shown a significant upward trend from 12.6 % in 1997 to 59.3 % in 2001.[10] Similar trends are reported in SGPGIMS, yearly statistics report about 15 % BCS. Newer surgical and diagnostic procedures are available only at a few select centers. As there are very few dedicated radiotherapy centers only 20% patients are offered Radiation therapy. The paucity of radiation therapy units is deterrent in setting up more BCS units. Tamoxifen is the most widely used hormonal therapy in our population. Assessment of histological grade is an important determinant of breast cancer prognostication.[17] Nottingham Grading System provides a simple, inexpensive, and highly accurate method for assessing tumor biological characteristics and patient prognosis. There is an international consensus that NGS should be considered the 'gold standard' for breast cancer grading.[18] In present study patients with NGS score <5 had > 60% five-year survival. NGS 6-7 had (38%) 5-year survival, but NGS 8-9 either presented with distant metastasis during initial presentation or developed distant metastasis within 3 years after primary treatment.

CONCLUSION

Breast cancer has emerged as the commonest cancer in Urban India, with second most common cancer in Rural India. Majority of our patients present with advanced disease stage with numerous poor prognostic factors such as young age, larger tumor size, lymph node metastasis, high pathological grade and poor hormone receptor status. These factors are a reflection of poor health awareness for breast cancer, general indifference towards women's health, poor financial resources, unavailability of multimodality treatment facilities. Though e.g. there is no shortage of skills and expertise in cytology, the use of fine needle aspiration cytology is underutilized and preoperative diagnosis is still based mainly on clinical, excisional or incisional biopsy.

Poor compliance to adjuvant/neoadjuvant chemotherapy in our population, has further resulted into treatment failures in terms of locoregional recurrences, poorer overall survival and also matters the quality of life. There are some encouraging outcomes at centers where world class healthcare is available. The recent emphasis by governmental agencies, institutions and non-governmental organizations (helping hand for cancer care) to provide a support for breast cancer screening, management as well as rehabilitation probably may help to improve the outcome. Limitation of our study, our institute is not equipped with the facility for Sentinel node biopsy, radiotherapy unit, chemotherapy facilities.

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