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Clinical profile and management of breast cancer in women in a rural based tertiary care hospital our experience

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ABSTRACT

Background: Breast cancer is the second most common cancer among women in India and accounts for 7% of global burden of breast cancer and one-fifth of all cancers among women in India. The risk factors are related to lifestyle, early menarche, nulli parity, prolonged use of oral contraceptive pills, hormone replacement therapy, not breast-feeding, alcohol, obesity, lack of exercise, and induced abortion. A woman who attains menopause after fifty five years of age has an increased risk of ovarian, breast, and uterine cancers. The risk is greater if a woman also began menstruating before twelve years of age. A longer exposure to estrogen increases a woman's risk of breast cancers.

Methods: This is a prospective observational study, conducted in the department of surgery, between December 2013 and June 2015(2 years). Patients diagnosed as breast carcinoma and admitted in surgical wards were included, Data pertaining to demography, clinical and pathological tumor profile, and treatment details were collected prospectively for each patient based on patient interviews and medical records. To analyse the Prevalence of breast cancer, clinical presentation, risk factors, diagnostic methods, treatment protocols, difference between pre and post-menopausal breast cancer women regarding risk factors, assess the impact of treatment given and women's knowledge about breast cancer.

Results: A total number of 25 cases of breast carcinoma based on detailed history, clinical examination, Trucut biopsy, ultrasonography breast and axilla, ultrasound abdomen, mammogram and chest x-ray were analysed. All of them received three cycles of anterior chemotherapy consisting of 5- Fluorouracil 500 mg/m2,Adriamycin 50 mg/m2 Cyclophosphamide 80 mg/m2 (FAC regimen) administered intravenously followed by modified radical mastectomy. There were no recurrences seen on follow up till date.

Conclusions: Late stage at presentation of breast cancer is a challenge to the health care providers. Cancer awareness programmes, multidisciplinary approach and evidence-based strategies for early detection and effective management of the disease can go a long way in prevention.

Keywords: Breast cancer, Indian women, Postmenopausal, Premenopausal, Risk factors

INTRODUCTION

Breast cancer is the most common female cancer worldwide. Global burden of breast cancer will increase to over 2 million new cases/year by 2030. The incidence

of breast cancer is rising in India (22.9%) and is now the second most commonly diagnosed cancer in women after cervical cancer. The age-standardized mortality rate for breast cancer in India was found to be 11.1/100,000 where globally it was 12.5/100,000 according to

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International Agency for Research on Cancer report in 2008. Although many risk factors may increase the chance of having breast cancer, it is not yet known just how some of these risk factors cause cells to become cancerous.1 Risk factors are gender, age, genetic factors, family history, dense breast tissue, menstrual periods, breast radiation early in life, pregnancy at late ages, use of birth control pills, hormone therapy, not breastfeeding, alcohol, obesity, lack of exercise, and induced abortion.^{2,3} The risk is greater if a woman attains menstruation before twelve years of age. Menopause after fifty five years of age has an increased risk of ovarian, breast, and uterine cancers. A longer exposure to estrogen increases a woman's risk of breast cancers. Therefore, women who have natural menopause are more likely to develop cancer twice high because of hormonal factors.3 Among all modalities of treatment available for ca breast surgery is the gold standard, complimented by other modalities. Chemotherapy in the treatment of breast cancer has assumed a greater significance as breast cancer is a systemic disease. Surgery can eradicate only the local disease, and eradication of the systemic component involves the use of chemotherapeutic agents, given either as an adjuvant, or Neo-adjuvant prior to surgery given in two to three doses.4

METHODS

Twenty five patients' female patients who were histologically or cytologically confirmed with breast cancer were included in the study between December 2013 and June 2015. Data on history and clinical presentation, ,staging, ultrasonography of breast and axilla, USG abdomen, mammogram, trucut biopsy, ER/PR/Her-2 neu and tumor characteristics, risk factors and chest x-ray and treatment modalities were collected as per proforma. Breast cancer was staged according to TNM staging and most of the patients were in stage IIb and IIIa, Patients were observed in two groups as premenopausal and postmenopausal. Patients who had cessation of menstrual flow for one year were considered as postmenopausal and the rest were considered as premenopausal. All of them received three cycles of anterior chemotherapy consisting of 5- Fluorouracil 500 mg/m2, Adriamycin 50 mg/m2 Cyclophosphamide 80 mg/m2 (FAC regimen) administered intravenously followed by modified radical mastectomy. Descriptive and inferential statistical analysis were done using SPSS software version 17.

RESULTS

In this study, the age at diagnosis ranged between 41to 80 years with a mean age of 54.24. More than half of the patients (54%) were diagnosed between the age of 40 and 60 years. About 36.0% were between 40-50 years and 20.0% were aged older than 60 years at presentation (Table 1). Nearly 68% patients were illiterates and 18% had primary education and the rest of 14% had secondary

education. Most of the patients were housewives and few were daily wage labors.

Table 1: Age distribution of patients.

| Age in years | No. of patients | % |
|--------------|-----------------|-------|
| 41-50 | 9 | 36.0 |
| 51-60 | 10 | 40.0 |
| 61-70 | 5 | 20.0 |
| 71-80 | 1 | 4.0 |
| Total | 25 | 100.0 |

Mean \pm SD: 54.24 \pm 8.21.

Table 2: Parity distribution.

| Parity | No. of patients $(n = 25)$ | % |
|-------------|----------------------------|------|
| Nulliparous | 4 | 16.0 |
| Multiparous | 21 | 84.0 |

Table 3: Menstrual status.

| Menstrual status | No. of patients (n = 25) | % |
|------------------|--------------------------|------|
| Premenopausal | 9 | 36.0 |
| Postmenopausal | 16 | 64.0 |

Table 4: Presenting complaints.

| Presenting complaints | No. of patients (n = 25) | 0/0 |
|-----------------------|--------------------------|-------|
| Lump | 25 | 100.0 |
| Ulceration | 0 | 0.0 |
| Pain | 16 | 64.0 |
| Nipple retraction | 0 | 0.0 |
| Nipple discharge | 3 | 12.0 |
| Axillary swelling | 0 | 0.0 |

Table 5: Duration of symptoms.

| Duration of symptoms | No. of patients (n = 25) | % |
|----------------------|--------------------------|------|
| <3 months | 7 | 28.0 |
| 3-6 months | 17 | 68.0 |
| >6 months | 1 | 4.0 |

Among 25 female patients, four were nulliparous 9 (16%) and 21 (84%) multiparous (Table 2), 9 (36%) were premenopausal and 16 (64%) had reached menopause (Table 3). 10 postmenopausal patients, attained menopause at age <45 years and 6 (58%) attained menopause at age >45 years. All patients presented with a lump in the breast. Pain nipple retraction and nipple discharge were present in some patients along with a lump in the breast (Table 4). 7 (28%) patients presented with a history of less than three months duration, 17 (68%) presented with history of 3-6 months and 1 (4%) presented with history of more than six months duration (Table 5). 15 patients had a lump in the right breast and 10 patients had a lump in the left breast. In the majority

of the patients, the lump was present in the upper outer quadrant.

Table 6: Quadrants involved.

| Quadrant involved | No. of patients | % |
|----------------------|-----------------|-------|
| Upper outer quadrant | 16 | 64.0 |
| Upper inner | 4 | 16.0 |
| Lower outer | 3 | 12.0 |
| Lower inner | 2 | 8.0 |
| Total | 25 | 100.0 |

Table 7: Tumor size at presentation.

| Tumor size before NAC | No. of patients (n = 25) | % | Mean ± SD |
|--------------------------|--------------------------|------|--------------|
| <5 cm | 13 | 52.0 | |
| <3 | 2 | 8.0 | |
| 3-4 | 10 | 40.0 | 3.35±0.94 |
| >4 | 1 | 4.0 | _ |
| 5-7 cm | 9 | 36.0 | |
| <5 | 0 | 0.0 | |
| 5-6 | 8 | 32.0 | 5.82±0.57 |
| >6 | 1 | 4.0 | |
| 7-10 cm | 3 | 12.0 | |
| 7.2 | 1 | 4.0 | |
| 7.8 | 1 | 4.0 | 7.93±0.81 |
| 8.8 | 1 | 4.0 | |

Table 8: Lymph node involved.

| Lymph node involved | No. of patients (n = 25) | % |
|---------------------|--------------------------|------|
| N0 | 6 | 24.0 |
| N1 | 11 | 44.0 |
| N2 | 8 | 32.0 |

Table 9: Stage of tumor.

| Stage of Tumor | No. of patients | % |
|----------------|-----------------|-------|
| IIB(T2N1M0) | 8 | 32.0 |
| IIB(T3N0M0) | 6 | 24.0 |
| IIIA(T1N2M0) | 1 | 4.0 |
| IIIA(T2N2M0) | 3 | 12.0 |
| IIIA(T3N1M0) | 3 | 12.0 |
| IIIA(T3N2M0) | 4 | 16.0 |
| Total | 25 | 100.0 |

Biopsy was the conformation test in all patients. Fine-needle aspiration cytology (FNAC) was done in all patients while core biopsy was done in 20 patients. Abdominal ultrasound, chest X-ray, complete blood count, and renal function tests were also done to all patients regularly as a part of diagnosis and for metastatic work up. Infiltrating duct cell carcinoma was the most prominent histopathological type seen in 20 (80%) cases in which 3 (12%) were premenopausal and 17 (68%)

were postmenopausal women. 5 (20%) postmenopausal women had lobular carcinoma. 11 (44%) patients were diagnosed with stage IIIB disease in which 3 were premenopausal and 22 were postmenopausal women. 14 (56%) patients were diagnosed with stage IIA 6 (24%) patients were pre and 8 (32%) postmenopausal women (Table 7, 8,). Majority of postmenopausal patients were progesterone positive, whereas the majority of premenopausal patients were estrogen positive. All of them received three cycles of anterior chemotherapy consisting of 5- Fluorouracil 500 mg/m2, Adriamycin 50 mg/m2 Cyclophosphamide 80 mg/m2 (FAC regimen), 84% patients responded and 16% showed no significant response. All 25 patients underwent modified radical mastectomy. Adjuvant radiotherapy was given to all postoperatively. Lymph edema of the upper limbs was noted in majority of patients post operatively. There were no recurrences on follow up till date.

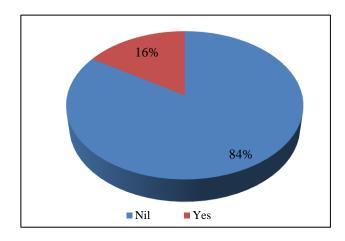


Figure 1: Pie chart showing tumor size reduction after anterior chemotherapy.

Table 10: Comparison of age distribution in various studies.

| Age groups | Current study | Sen and Dasgupta series | Chopra R | Goel A et al |
|----------------|----------------------|-------------------------------|-------------|-----------------|
| 31-40 years | - | 23.8% | 18.0% | 40% |
| 41-50 years | 36% | 36.9% | 32.5% | 20% |
| 51-60 years | 40% | 25.2% | 25.8% | 15% |
| > 60 years | 24% | 11.4% | 20.0% | 15% |

Table 11: Comparison of menstrual status in different studies.

| Menstrual status | Current study | DS Sandhu Amit | Aggarwal et al | Karlsson YA et al. |
|---------------------|---------------|----------------------|-------------------|--------------------------|
| Premenopausal | 36% | 44.24% | 56% | 41% |
| Postmenopausal | 64% | 55.76% | 4% | 59% |

DISCUSSION

In this study 44% of the female patients admitted for the treatment of breast cancer were locally advanced. Chopra R states the proportion of LABC to the total number of reported breast cases to be 28.9%, 40.5% and 52% in Mumbai, Trivandrum and Chennai respectively. The proportion of LABC is very high in developing countries compared to the western countries. Locally advanced breast cancer is a very common clinical scenario especially in developing countries (30-60%) possibly due to various factors like lack of medical facilities, education, awareness and poor socio-economic status. Late diagnosis is a major factor for increased mortality as the majority of the patients present in advanced or metastatic stage.^{8,9} The mean age in our study was 54.2 years which is different from Aggarwal A et al and DS Sandhu et al which was 46.5 years and 47.39 years (Table 10, 11). 10,11 In general, breast cancer has been reported to occur a decade earlier in Indian patients compared to their western counterparts. The presenting features are compared with some of the similar series from India. Most of the cases present with 3-6 months duration. The percentage of patients in this range was 68% and 32.9% in our study and in Sandhu DS et al series respectively. The cases with less than 3 months duration were higher in Sandhu DS series compared to our study. Jaiganesh Vishambaran LK et al reported N0 to be 2%, N1 stages to be 91% and N2 stages to be 7%. Compared to this study our patients showed a higher incidence of N1 disease. Same results seen in Chintamani et al (Table 10, 11). Most common stage in Indian population is stage III. In our study we have included only the patients who have presented with stages of IIB and IIIA. The age of the patients ranged from 41 to 80 years. The highest number of patients were in the age group of 51-60 years age group with 40% (10 patients), followed by 41-50 years age group with 36% (9 patients). The mean age of patients was 54.2 years. The highest numbers of cases were seen in the age group of 51-60 years, other studies showing highest incidence in age group in 41-50 years except in Goel A et al the peak is seen in 31-40 years age group. Some previous studies stated that breast cancer is a disease of older women and its incidence increases with age, and it is rare below the age of 20 years. Majority of patients in our study were between the fourth and fifth decade of life similar to studies reported from India and other Asian countries.10

A majority of premenopausal patients were in third and fourth decade of life and the postmenopausal were in fifth and sixth decade of life. More than 50% of women included in the study were diagnosed before the age of 50 years, in contrast to the western settings where only 23% of women younger than 50 years presented with breast cancer While the majority of breast cancer patients in western countries are postmenopausal and in their 60s and 70s, the picture is quite different in India with premenopausal patients constituting about 50% of all patients. Majority of the patients were from a rural

background, The incidence of breast cancer in this study was found slightly more in postmenopausal women than in premenopausal women.

In postmenopausal women majority of them attained menopause after the age of 45 years. Some studies reported that younger age at menarche increased breast cancer risk only in premenopausal women, while some reported increased risk only for postmenopausal women. In some studies done previously, age at menarche was be associated with both post-menopausal breast cancer while in another studies, it had no association with either pre- or post-menopausal breast cancer. 12,13 In this study, early onset of menarche was found to be associated with both pre and postmenopausal patients as the majority of the patients in either groups attained puberty at an age of <12 years. The median age of menarche worldwide is 14 years with a range from 11 to 18 years. Some studies done on Indian women showed that the risk of both premenopausal and postmenopausal breast cancer decreased with delay in the onset of menarche. 14 Late menopause increases the risk of breast cancer. Postmenopausal women have a lower risk of breast cancer than premenopausal women of the same age and childbearing pattern.

Risk increases by almost 3% for each year older at menopause thus women who have attained menopause at 55 years rather than 45 years, has approximately 30% higher risk. In this study, majority of the women reached menopause after the age of 45 years. Risk of developing breast cancer increased in both pre-and post-menopausal patients who had early onset of menarche and late menopause possibly due to the increase in the duration of hormonal exposure15. In our study more patients were postmenopausal 64% (16 patients) than premenopausal 36% (9 patients). Similar profile can be seen in Karlsso N YA et al series. In Sandhu DS et al study 44.27% of the patients were premenopausal and 55.76%. Karlsson YA al reported 41% premenopausal and 59% postmenopausal. 11,15 Compared to the west the percentage of premenopausal patients are less in this study. Early age at first full-term pregnancy is inversely related to breast cancer risk. This association perhaps reflects either a pregnancy induced maturation of mammary cells, and thus making them less susceptible to carcinogenic transformation or a long lasting hormonal change or both. In this study, it was found that the majority of the women were at an age younger than 30 during their first pregnancy. However, information regarding the age at last pregnancy was not clear. Late age at last full term pregnancy also has been found to be associated with a higher risk of breast cancer, but not in all studies. High parity has generally been associated with low breast cancer risk in previous epidemiological studies. Nulliparity was associated with an overall increased risk of breast cancer. In our study it was found that many women presented with breast cancer despite of high parity.16

Practicing breast feeding was believed to minimize the risk of breast cancer in both pre and postmenopausal patients. The longer the duration of breastfeeding by women, the greater protection and the risk is relatively reduced by 4% for every 12 months of breastfeeding.¹⁷ But in our study, we noted that breast feeding was not protective against breast cancer in both pre and postmenopausal women, which was seen in the majority of the western studies. Studies done in India to examine the relationship between breastfeeding and breast cancer risk has shown mixed results it reported that increased duration of breastfeeding was associated with a significantly decreased risk of premenopausal breast cancer, but no effect was seen in women with postmenopausal breast cancer.

A study done in Mumbai showed a non-significant protective effect for breast feeding. But due to small sample size of this study, results were probably underpowered to detect significant differences. One study done in China reported that induced abortion was associated with an increased risk for breast cancer and with a dose-response relationship. In this study, also similar finding was observed, but more studies should be done to prove it significantly.¹⁸ Most of the patients, both pre-and post-menopausal patients had dense breast tissue. Dense breast tissue means there is more glandular tissue and less fatty tissue that is associated with epithelial proliferation and stromal fibrosis. Breast cancers originate in epithelial cells, so greater areas of fibro glandular tissue may reflect a greater number of cells that are at risk of carcinogenesis and/or an increased rate of epithelial proliferation.

Dense breast tissue can also make it difficult to interpret on mammogram. The data from Indian studies overall suggests that the role of known risk factors on the development of breast cancer within the Indian population is unclear and a large multicenter study would be of benefit to try and understand the shifting trends in breast cancer incidence in the population 19. The nature of disease presentation and tumor characteristics were found independent of the menopausal status and were related to the stage of the disease. Lump in the breast was the chief presenting complaint of all the women in this study as reported in various studies. The incidence of breast cancer was more in the upper and central quadrants of either side probably because of larger volume of breast tissue present in those quadrants. The most consistent symptom is that of a lump and is seen in all cases in our study and 87.9%, 74%, 96.5% in Sandhu DS et al, Gang et al and Raina et al series respectively. The percentages of lump in the upper outer quadrants are 64%, 47%, 49% and 48% in the current, Sandhu DS et al, Sen and Dasgupta et al and Fields et al series. No patient presented with isolated complaint of pain or nipple discharge or nipple retraction. During patient interview, it was found that almost all women found a lump in their breast by themselves, but due to lack of knowledge about breast cancer they were not able to detect their disease 20.

The problem of late presentation is mainly due to rural background, poverty and lack of awareness.

For the diagnosis of breast carcinoma, FNAC was done in all patients while core needle biopsy was done in twenty of the patients and a positive predictive outcome. Apart from these tests abdominal ultrasound, chest X-ray, complete blood count, harmonal assay, renal function tests and cardiac tests were done for metastatic workup. As reported in most of the previous studies, infiltrating ductal carcinoma was the prominent histopathological type, followed by lobular, medullary.²⁰ All of them were in locally advanced stage due to lack of awareness of the disease. Assessment of hormonal status and lymph nodes was useful in determining treatment and also for prognostication. Most of the patients were found either estrogen positive or progesterone positive. Intensive use of chemotherapy is indicated from 4 to 12 cycles in invasive breast cancer. All the patients irrespective of their stage of disease received three cycles of neo adjuvant chemotherapy (CMF) followed by modified radical mastectomy and adjuvant chemotherapy. Hormonal therapy was not continued by the patients due to low economic status. 25 patients with breast cancer received single cycle of Neo-adjuvant chemotherapy with 5-Flurouracil, Cyclophosphamide and Adriamycin. Our study shows that following neo-adjuvant chemotherapy there is decrease in tumor size among 16% with down staging among 12% of cases, the observation made here is decrease in tumor size is seen in patients with no axillary metastasis and with multiparous women.

CONCLUSION

Treatment of breast cancer should be multi-disciplinary. Educating the women on self-breast examination and screening techniques, can help in early diagnosis of the disease. Hence, public health programs that ensure access to appropriate, affordable diagnostic tests and treatment must be implemented.

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institutional ethics committee

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