

RESEARCH ARTICLE

A Retrospective Analysis of Incidence of Breast Cancer at a Tertiary Care Hospital in South India

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Abstract

Breast cancer occupies the peak position among other women cancers in Indian scenario. However, regional specific epidemiological data are inadequate. In this retrospective study, 142 patients were diagnosed as breast cancer positives and most of them fall within the age group of 20-50 years. Left sided cancer was more apparently seen in the positives cases. The highest frequency of cases was noticed in BIRADS grade 2, followed by grade 4. Receptor positivity was found to be 30.77% (ER), 23.07% (PR) and Her2/neu (26.15%). Seven out of 142 positive cases were diagnosed as locally advanced metastatic breast cancer. This study concludes that incidence of breast cancer with malignancy nature has been prevalent among fertile age of women. This age shift needs to be taken into account for future perspective of drug discoveries.

Keywords: Breast cancer, incidence, metastatic, Her2/neu, pre-menopausal.

Introduction

Breast cancer showed an epidemic episode confronted by developing countries in recent era, which was evidenced by several prospective studies (Anderson, 2008). Large number of entries was augmented in breast cancer around the globe in past decades (Hortobagyi, 2005; Anderson, 2008; Porter, 2008). According to the International Agency for Research on Cancer (IARC), about 20-30% increase in the incidence of breast cancer have been noticed in developing countries (Khokhar, 2012) and it was anticipated that an increase in the incidence would be climb up to 26% in 2020 (Wong, 2009). A study published by Green *et al.* (2008) showed that women in Asian countries were highly prone to breast cancer even in their forties. In our country, breast cancer has taken the lead over all other cancers (Ambrose *et al.*, 2011; Fitzmaurice *et al.*, 2015). Age is one among the strongest risk factor not only in early diagnosis of a disease but also in therapeutic perceptions (Sasieni *et al.*, 2011). According to the ICMR-PBCR data, the incidence of breast cancer in India has markedly increased in all regions and in every age group (National Cancer Registry Programme, 2001), whereas, the mean age for breast cancer varies between different regions. The incidence of breast cancer in pre-menopausal women constitutes ~13% in the age group between 20-44 years (Mir and Singh, 2009; Hickey, 2009). A considerable proportion of Indian breast cancer patients were in the age of less than 35 years (Agarwal *et al.*, 2007). Breast cancer in pre-menopausal women has several complications, including fertility, conception and breast feeding. The status of the hormonal receptor such as estrogen receptor (ER), progesterone receptor (PR), and epidermal growth factor receptor 2 (Her2/neu) plays a pivotal role in determining the stages and/or severity of the breast cancer.

Breast cancer patients can be classified based on the positivity of one or both of the endocrine receptors and some of them may be triple positive (positive for ER, PR and Her2/neu). The triple negative breast cancer is the biologically aggressive form compared to other sub-types of breast cancer because of unresponsiveness to the conventional chemotherapy treatment (Kakarala *et al.*, 2010). Moreover, breast cancer can be commonly classified as non-invasive (Benign) and invasive (Metastatic) which depends on the spreading of the cancer cells. The combination of either of this stage, along with the receptor positivity makes the breast cancer a heterogeneous disease. Even though Her2 protein was considered as metastatic marker for breast cancer, some exceptional cases were there in the cancer registry. Several chemotherapy drugs are targeted for the molecular signaling pathways in order to reduce the receptor gene expression and/or its activation. Fertility issues on post-chemotherapy seems to be the most considered among the pre-menopausal women. Common effects of chemotherapy were induced ovarian dysfunction that includes depletion of primordial follicle and interference in the follicular maturation and temporary or permanent menopause in a dose dependent manner (Oktay *et al.*, 2006; Oktem and Oktay 2007). Hence, there is an urgent need for studies focused on the chemotherapy prescribed for pre-menopausal women affected with metastatic breast cancer. Till date, no other studies have focused the percentage of positivity in Her2 receptor among pre-menopausal age group in south India population. This present retrospective investigation was aimed to figure out the incidence of breast cancer and metastatic condition among pre-menopausal women and to analyse the hormonal status in the age group between 20-45 years.

Materials and methods

Study population and experimental design: The cancer patients obtained treatment in Harshamitra Cancer Center, Tiruchirappalli, Tamil Nadu, India, during the period from Jan 2012 to Dec 2012 were included in this study and their case reports were analysed for the history of the disease. This study has been done according to the standard ethics and by maintaining the confidentiality of reports. Among the total cancer patients case report, patient's with known visual as well as cytological abnormalities in their breast and prescribed for breast cancer screening were focused for next level investigation. The case history showed several methods including visual examination of breasts, mammogram examination, histological examination and molecular analysis for determination of receptor positivity. Receptor status was confirmed by immuno-histochemical staining method by which weak positive cases, i.e. less than 10% of stained cells, were considered as negative. All the breast cancer case reports were segregated based on their age group, tumor grade and receptor positivity.

Statistical analysis: Descriptive analysis was carried out in MS Excel 2007 and SPSS version 11.5 software (SPSS Inc., Chicago, IL) for data analysis.

Results

From a total population of 511 cancer patients, 252 cancer patients who had visited the hospital for breast cancer diagnosis were included for this retrospective study. Visual examination accompanied with cytological and/or histological analysis revealed only 56.35% (142 cases) of the patients were diagnosed as breast cancer patients, of which 76.06% cases were on benign stage and 23.94% cases were on metastatic stage. The proportion of positive cases with respect to their age groups was shown in Fig. 1. Age group of the total positive cases ranged from 20 to 85 years with an average age of 45.42±12.21. The highest number of breast cancer cases falls on the age group of 41-50 years (33.1%), followed by 31-40 years (27.8%) and 51-60 years (20.4%). The number of women suffering on breast cancer at an age less than 48 years i.e. in pre-menopausal period was 79, where rest of the 63 cases are above 48 years. A high percentage (81.7%) of cancer was localization as unilateral, of which 65 cases were left oriented and 51 cases possess cancer in their right breast (Fig. 2). In general (n= 252), the vast majority of mammogram patients were categorized under BIRADS 1 and 2 as shown in Table 1. Among positive case reports, predominant tumors were of grade 2 (39.44%) and grade 4 (21.83%). A total number of 65 cases (both BIRAD IV and V) out of 142 positive cases were reported to be analyzed for receptor status, where ER, PR and Her-2/neu expressions were observed in 30.77, 23.07 and 26.15% of the cases whereas, 20% of triple negative cases were noticed.

Fig. 1. Distribution of breast cancer cases among different age groups of South Indian women.

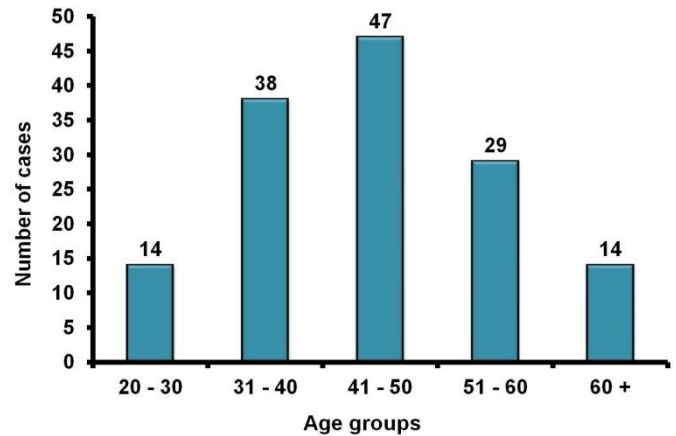


Fig. 2. Orientation of cancer in breast cancer patients.

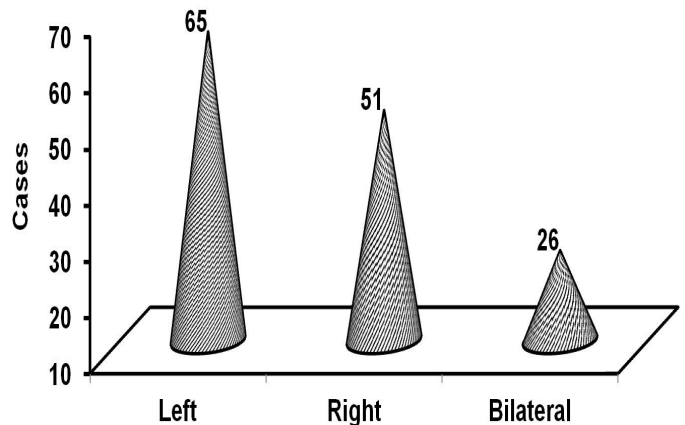


Fig. 3. Pictorial representation of number of breast cancer cases in different categories.

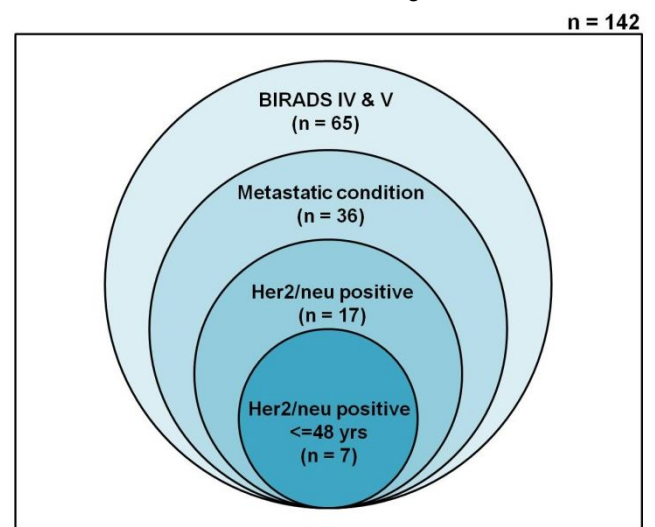


Table 1. Screening of patients based on their mammographic results.

BIRADS category scale	Number of patients
1 (negatives)	110
2 (Benign)	56
3 (Probably benign)	29
4 (Suspicious)	31
5 (Highly suggestive of malignancy)	26
6 (proven malignancy)	17

Table 2. Her2/neu receptor status with respect to fertility status of women.

Fertility status	Age group (years)	Her2/neu status in BIRADS IV and V			P value
		Negative (n=48)	Positive (n=17)	Odds ratio (OR)	
Fertile	20-48	16 (66.7%)	8 (33.3%)	2.00	<0.100
	48-60	25 (83.3%)	5 (16.7%)	-	
Non-fertile	>60	7	4	-	-

Steroid receptors (both progesterone/estrogen) were found to be in one fourth (24.6%) of the total positive cases. Moreover, the presence of Her2/neu was witnessed twofold higher in the age group of 20 to 48 years than above 48 years of age. Among 65 cases that have been checked for Her2/neu receptor status, in that only 26.15% showed positive, whereas this percentage was mostly associated with the metastatic condition (Fig. 3). In the age group of <45 years an over-expressed Her2/neu receptor was reported in 10.8% of the metastatic cases (Table 2). Association of Her2/neu status and other steroid hormonal status is significantly ($p < 0.001$) correlated in the age group of 20-48 years. This present study showed the incidence of breast cancer in the age group between 20 and 48 years with a multi-dimensional view including their metastatic condition, occurrence of the steroid hormones receptor and Her2/neu receptor status in the biopsy tissue.

Discussion

Several published studies have illustrated the incidence of breast cancer in Indian scenario. A study conducted by Sinha (2012) revealed that the breast cancer in the age group of 30-35 years constitutes about 77% followed by 24% in age group of 25-29 years. The present study showed a high incidence of cases in the age group of 25-50 years. The statistical analysis of cases crowded near the range of 20-48 years was conducted with the reference of Baria (2012) who specified that the average age of menopause was 48 years in Indian women. Hence, for this present study, the cases ≤ 48 years were considered as pre-menopausal women. Several chemotherapies provided to such pre-menopausal women might lead to irreversible fertility issues. Therefore, we carried out this study to bring out the Her2/neu receptor statuses in metastatic cases of 20-48 years of age group. The mean age of patients in our study was 45.42 ± 12.21 years which were in comparable with studies conducted by Sharif *et al.* (2009) and Azizun-Nisa *et al.* (2008). However, the mean age of population studied in western countries showed a higher value (Kakarala, 2010).

Yu *et al.* (2012) studied a large Chinese population and reported that 60% of cancer constituted for pre-menopausal women as that of 55.6% presented in our study. Left oriented breast cancer showed 45.8% positivity having a 10% lead when compared to the right orientation and this was in consonance with Tulinius *et al.* (1990) report. Wilting and Hagedorn (2011) showed that the left side of the body is prone to carcinomas, especially breast cancer (5-10%). The percentage of Her-2 positive data varied from 16 to 27% all over the world (Owens *et al.*, 2004; Azizun-Nisa *et al.*, 2008; Sharif *et al.*, 2009). Konecny *et al.* (2003) studied two populations, Germany and South Australia and reported 67.2 and 70.2% was positive for ER receptor and 67.5 and 66.4% was positive for PR receptor, respectively. An overall steroid hormone receptor positive case was reported to be 41.5%. The presence of Her/neu 2 receptor positive cases was reported more in BIRAD grade 4 conditions (Table 2). This result was in contradictory with previous studies in which the percentage of positivity varied from 6.7-29.9% of grade 1 to 3, respectively (Taucher *et al.*, 2003; Lal *et al.*, 2005).

Conclusion

Ample number of research articles has been published continuously which portrays the current scenario of breast cancer. Interestingly, this statistical data clearly depicts the current percentage of breast cancer survivors after chemotherapy lies primarily in the young women. Younger women show greater involvement in their treatment decision-making than older women. Hence, the clinicians have to give prior counseling before and after chemotherapy regarding the possible outcome of the treatment and the fertility issues. Moreover, early detection and timely treatment of breast cancer has been shown to improve survival rates in younger age women. Therefore, attention has to be put forth to raise public awareness not only on older women but also to younger generation who appear to have higher risk of breast cancer.

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References

1. Agarwal, G., Pradeep, P.V., Aggarwal, V., Yip, C.H. and Cheung, P.S. 2007. Spectrum of breast cancer in Asian women. *World J. Surg.* 31(5): 1031-1040.
2. Ambroise, M., Ghosh, M., Mallikarjuna, V.S. and Kurian, A. 2011. Immunohistochemical profile of breast cancer patients at a tertiary care hospital in South India. *Asian Pac. J. Cancer Prev.* 12(3): 625-629.
3. Anderson, B.O. and Jakesz, R. 2008. Breast cancer issues in developing countries: an overview of the breast health global initiative. *World J. Surg.* 32(12):2579-2585.
4. Azizun-Nisa, Bhurgri, Y., Raza, F. and Kayani, N. 2008. Comparison of ER, PR and HER-2/neu (C-erb B 2) reactivity pattern with histologic grade, tumor size and lymph node status in breast cancer. *Asian Pac. J. Cancer Prev.* 9(4): 553-556.
5. Baria. Z. 2012. Premature menopause on the rise. Retrieved from The Times of India, Nov 2.
6. Fitzmaurice, C., Dicker, D., Pain, A., Hamavid, H. and Moradi-Lakeh, M. 2015. The Global Burden of Cancer 2013. *JAMA Oncol.* 1(4): 505-527.
7. Green, M. and Raina, V. 2008. Epidemiology, screening and diagnosis of breast cancer in the Asia-Pacific region: current perspectives and important considerations. *Asia Pac. J. Clin. Oncol.* 4(S3): 5-13.
8. Hickey, M., Peate, M., Saunders, C.M. and Friedlander, M. 2009. Breast cancer in young women and its impact on reproductive function. *Hum. Reprod. Update.* 15(3): 323-339.
9. Hortobagyi, G.N., Garza, S.J., Pritchard, K., Amadori, D., Haidinger, R., Hudis, CA., Khaledg, H., Liu, M.C., Martini, M., Namerj, M., O'Shaughnessy, J.A., Shenl, Z.Z. and Albain, K.S. 2005. The global breast cancer burden: variations in epidemiology and survival. *Clin. Breast Cancer.* 6(5): 391-401.
10. Kakarala, M., Rozek, L., Cote, M., Liyanage, S. and Brenner, D.E. 2010. Breast cancer histology and receptor status characterization in Asian Indian and Pakistani women in the U.S.-a SEER analysis. *BMC Cancer.* 10: 191.
11. Khokhar, A. 2012. Breast Cancer in India: Where Do We Stand and Where Do We Go?- A mini-review. *Asian Pac. J. Cancer Prev.* 13: 4861-4866.
12. Konecny, G., Pauletti, G., Pegram, M., Untch, M., Dandekar, S., Aguilar, Z., Wilson, C., Rong, H.M., Bauerfeind, I., Felber, M., Wang, H.J., Beryt, M., Seshadri, R., Hepp, H. and Slamon, D.J. 2003. Quantitative association between HER-2/neu and steroid hormone receptors in hormone receptor-positive primary breast cancer. *J. Natl. Cancer Inst.* 95(2): 142-153.
13. Lal, P., Tan, L.K. and Chen, B. 2005. Correlation of HER-2 status with estrogen and progesterone receptors and histological features in 3,655 invasive breast carcinomas. *Am. J. Clin. Pathol.* 123(4): 541-546.
14. Mir, R. and Singh, V.P. 2009. Breast cancer in young women and its impact on reproductive function. *Apollo Med.* 6(3): 200-208.
15. National Cancer Registry Programme: Consolidated report of the population based cancer registries 1990-1996. Indian Council of Medical Research, New Delhi, 2001.
16. Oktay, K., Oktem, O., Reh, A. and Vahdat, L. 2006. Measuring the impact of chemotherapy on fertility in women with breast cancer. *J. Clin. Oncol.* 24(24): 4044-4046.
17. Oktem, O. and Oktay, K. 2007. Quantitative assessment of the impact of chemotherapy on ovarian follicle reserve and stromal function. *Cancer.* 110(10): 2222-2229.
18. Owens, M.A., Horten, B.C. and Silva, M.M.D. 2004. HER2 amplification ratios by fluorescence in situ hybridization and correlation with immunohistochemistry in a cohort of 6556 breast cancer tissues. *Clin. Breast Cancer.* 5(1): 63-69.
19. Porter, P. 2008. Westernizing women's risks? Breast cancer in lower-income countries. *N. Engl. J. Med.* 358: 213-236.
20. Sasieni, P.D., Shelton, J., Ormiston-Smith, N., Thomson, C.S. and Silcocks, P.B. 2011. What is the lifetime risk of developing cancer? The effect of adjusting for multiple primaries. *Br. J. Cancer.* 105(3): 460-5
21. Sharif, M.A., Mamoon, N., Mushtaq, S. and Khadim, M.T. 2009. Morphological profile and association of HER-2/neu with prognostic markers in breast carcinoma in Northern Pakistan. *J. Coll. Physicians Surg. Pak.* 19(2): 99-103.
22. Sinha, K. 2012. Breast cancer becoming common among 30-year-old Indian women: Study. Retrieved from The Times of India, Feb 26, p.54.
23. Taucher, S., Rudas, M., Gnant, M., Thomanek, K., Dubsy, P., Roka, S., Bachleitner, T., Kandioler, D., Wenzel, C., Steger, G., Mittlbock, M. and Jakesz, R. 2003. Sequential steroid hormone receptor measurements in primary breast cancer with and without intervening primary chemotherapy. *Endocrine-Related Cancer.* 10: 91-98.
24. Tulinius, H., Sigvaldason, H. and Olafsdóttir, G. 1990. Left and right sided breast cancer. *Pathol. Res. Pract.* 186(1): 92-94.
25. Wilting, J. and Hagedorn, M. 2011. Left-right asymmetry in embryonic development and breast cancer: common molecular determinants? *Curr. Med. Chem.* 18(36): 5519-5527.
26. Wong, N.S., Anderson, B.O., Khoo, K.S., Ang, P.T., Yip, C.H., Lu, Y.S., Voravud, N., Shao, W.M. and Pritchard, K.I. 2009. Breast cancer in developing countries. *Lancet.* 10(11): 1077-1085.
27. Yu, Z.J., Jia, C.X., Liu, L.Y., Geng, C.Z., Tang, J.H., Zhang, J., Zhang, Q., Li, Y.Y. and Ma, Z.B. 2012. The prevalence and correlates of breast cancer among women in Eastern China. *PLoS One.* 7(6): e37784.