



THE STUDY OF EPIDEMIOLOGICAL FEATURES OF BREAST CANCER IN PUBLIC SECTOR CANCER CARE CENTRE IN NORTHERN INDIA

Oncology

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ABSTRACT

Introduction: Breast cancer occurrence in India has rapidly risen to overtake cervical cancer in terms of incidence as well as mortality. Breast cancer is considered to be a complex disease demonstrating heterogeneity at clinical and histopathological levels. We believe that Breast cancer in the Indian population could be biologically different from those of the west. We attempt to study the clinical & pathological aspects of breast cancer with comparison to the western population in order to find pattern of differences.

Materials and methods: All patients diagnosed and treated in the department of surgical oncology, King George Medical University, Lucknow, UP from the period of August 2014 to August 2016 are included. Clinical and histopathological data was recorded.

Results: A total of 355 patients were analyzed. Average age of patients with disease was 45.3yrs. The premenopausal group consists of 52% of patients. Mostly patients presented in locally advanced stage.

Conclusion: As compared to the western population the breast cancer in India presents in younger, premenopausal, multiparous and breast feeding women. They present in locally advanced stages with higher nodal positivity rates. It appears to be that breast cancer in India is a different subset from the western world in having different molecular signatures that translates into distinct clinical and histopathological subgroup.

KEYWORDS

Breast cancer, Indian, west, epidemiology

INTRODUCTION

Breast cancer is one of the major health problem for women all across the globe.[1,2] In the United states Breast cancer would account for almost one third of all female cancers. It is also the second leading cause of cancer death among women after lung cancer. Since 1999, incidence rates of breast cancer have stabilized in women in US with only a slight rise with continuous drop in number of deaths due to the disease. Despite the falling rates, Female breast cancer represents 14.6% of all new cancer cases in the U.S. [2].

The incidence rate of breast cancer has stabilized over the period of time with most occurring in old age postmenopausal females. Majority of these patients would be detected at an early stage. Indian Breast cancer represents a dramatically different picture.

Breast cancer in India is rapidly expanding overtaking cervical cancer in terms of incidence as well as mortality. Indian women with Breast cancer are younger, premenopausal and a large proportion of patients present at advanced stages. Considering Breast cancer to be a complex disease demonstrating heterogeneity at clinical and histopathological levels, breast cancer in the Indian population could be biologically different from those of the west.

In India, breast cancer incidence has already been rising rapidly over last ten years to alarming proportions to overtake cervical cancer in terms of most common cause of cancer. The disturbing aspects of breast cancer is epidemiology which includes the facts of breast cancer becoming also the most common cause of cancer related mortality in females where almost every 2nd woman due to breast cancer in India will die due to the disease. Also worrisome is the incidence of breast cancer on rise in younger population with almost half the cases occurring in females less than 50. [3]

According to recent studies in US on Indian patients and some Indian studies breast cancer in our population may be biologically different in terms of age at presentation, response to chemotherapy and prognosis. Understanding frequency of specific breast cancer subtypes and associate risk factors may better elucidate breast cancer treatment strategies for Indian population.

We attempt to study the clinical & pathological aspects of breast cancer with comparison to the western population in order to find pattern of

differences.

MATERIALS AND METHODS

This study included a total of 355 patients of breast carcinomas diagnosed in our department from August 2013 to November 2016. All of the patients were diagnosed and treated in department of surgical oncology, King George Medical University, Lucknow, UP. For all patients, clinical and histopathological informations were noted in detail in specified proforma.

Histopathology Sample comprised of either tissue obtained by tru-cut, incisional, excisional or post-surgical specimen from patients. After collection the samples was sent for histopathological evaluation at Department of Pathology K.G.M.U.

Histopathological categorization of breast carcinoma was done under College of American Pathologists (CAP) protocol which included the diagnostic information such as -specimen identification procedure, laterality, lymph node sampling, site and size of the tumour, histological type, tumour grading under the Nottingham modification of the Bloom-Richardson system and evaluation of prognostic histopathological parameters.

Because this was not a clinical trial, the patient population was diverse and the treatment received by patients was variable. NACT and Palliative CT given to the patients were mainly based on clinical staging and physician discretion. The type of therapy given can be broadly classified as anthracycline-based. Therapy, that is doxorubicin (Adriamycin) plus cyclophosphamide, 5-fluorouracil, epirubicin, and cyclophosphamide, or taxane-based therapy,

CLINICAL OUTCOMES

Response assessment to chemotherapy was done using the Recist criteria Complete Response (CR): Disappearance of all target lesions. Any pathological lymph nodes (whether target or non-target) must have reduction in short axis to <10 mm.

Partial Response (PR): At least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum diameters.

Progressive Disease (PD): At least a 20% increase in the sum of diameters of target lesions, taking as reference the smallest sum on

study (this includes the baseline sum if that is the smallest on study). In addition to the relative increase of 20%, the sum must also demonstrate an absolute increase of at least 5 mm. (Note: the appearance of one or more new lesions is also considered progression).

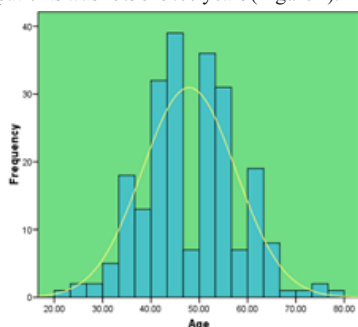
Stable Disease (SD): Neither sufficient nor shrinkage to qualify for PR nor sufficient increase to qualify for PD, taking as reference the smallest sum diameters while on study.

Variables were evaluated and analyzed statistically. Chi-square (χ^2) and Student t tests were used to compare variables and tests were considered significant when P-Value < 0.05.

RESULTS

The present study was carried out with an aim to carry out an immunohistochemical (IHC) study of breast cancer cases and to correlate IHC findings with clinicopathological profile and outcome. For this purpose, a total of 355 patients falling in sampling frame were enrolled in the study.

Age of patients ranged from 21 to 80 years. The age frequency curve indicated that the high proportion of younger population is having the disease. Almost 2/3rd of the population was under 50 years of age. Mean age of patients was 45.38 ± 9.67 years (Figure 1).



Out of a total of 355 patients enrolled in the study, 346 were women and 9 were men. Among women, 188 (52.9%) were in pre-menopausal stage of their life whereas remaining 158 (45.1%) of women were in pre-menopausal stage of their life. Except for 5 (1.8%) nullipara women, all the female patients were parous.

Nodal positivity rate was 54% (Table 1).

Table 1

Clinical Stage		
Early	134	38.1%
LABC	157	44.6%
Metastatic	61	17.3%
Nodal Postivity		
Yes	190	54.00%
No	162	46.00%

The premenopausal patients presented significantly more in locally advanced and metastatic stages as compared to post-menopausal women. ($p=0.0173$).

The response rates to neoadjuvant chemotherapy in our population was quite low with pathological complete response achieved in only 8.5% of the patients. Majority of patients of patient showed a partial response that consisted of 47% of the patients. Almost 44.6 % of patients did not show any response to chemotherapy with having either stable or progressive disease.

In our study period 17 patients had a recurrence out of 178 surgically treated patients giving a recurrence rate at the end of two years as 9.55%. Mean Disease free interval came out to be 11.86 months. Mean progression free survival was 7.54 months.

DISCUSSION:

Our study showed that almost 2/3rd of the population was under 50 years of age. Mean age of patients was 45.38 ± 9.67 years. The age frequency curve indicated that the high proportion of younger population is having the disease. This is in contrast with the west, the mean age of occurrence of breast cancer in the US is 62 years.[2] The frequency curves indicate the differences in the occurrence of cancer

where in west the disease is occurring in old age patients .[2] In the study by Onitilo et al [4] mean age of all subjects was 62.7 years (SD, 13.8; range, 27.9 to 95.8 years). In study by Manjunath et al conducted in India [5] the mean age was 53.0 years, with 76.4% (191 of 250) being less than 60 years of age. It appears to be that the breast cancer occurrence in India is almost a decade earlier than occurring in the west.

In our study we found that 52.9% of the breast cancer patients were Postmenopausal and 44.4 % of the people were premenopausal patients whereas almost 3% of the patients were males. This represents a very high status of premenopausal patients having breast cancer.

In the analysis of SEER data by Kakala et al [6] revealed that percentage of postmenopausal patients in the US is 75.5%. But the subgroup analysis of Indian and Pakistani population of patients showed that percentage of postmenopausal women having Breast cancer was 53.9% which is comparable to our study.

Our study also revealed another disturbing fact that only 38.7% of the patients presented at early stage whereas about locally advanced and metastatic patients contributed to 40.4 % and 20.9% respectively Western patients mostly present with early stage breast cancer. According to SEER data [2] 61% of patients would present at early stage, 31% of the patients at the locally advanced stage and only 6% of the patients would present at metastatic stage. Kakala et al in his analysis [6] showed in Caucasian American women almost 88.5 % presented with early breast cancer.

The higher proportion of breast cancer patients presenting late in our centre is worrisome issue. The most important reason for this can due to both lack of awareness of breast cancer as well as lack of screening programmes for breast cancer. Due to robust screening programmes in the west has lead marked reduction in late diagnosis of cancer as well as mortality rates.

In our study neoadjuvant chemotherapy given to the patient usually comprised of 3-4 cycles of FEC. Response were assessed after the end of 3 cycles of chemotherapy.

Pathological complete response was achieved in only 8.5% of the patients which is quite low. Majority of patients formed the partial response group which consisted of 47% of the patients. Almost 44.6 % of patients did not show any response to chemotherapy with having either stable or progressive disease.

Bhargav et [7] analyzed the NACT database and tried to identify the molecular classes (using IHC surrogate markers) that predict complete pathologic response to NACT Of the 359 cases that could be classified using IHC surrogate markers, 48 cases (13%) demonstrated complete pathologic response. The highest rate of complete pathologic response was seen in ERBB2 and triple-negative tumor classes with 33% (19 of 57) and 30% (24 of 79) showing complete pathologic response, respectively.

Similar study by Rouzier et al [8] showed complete response rate of 13.41 % in their patients. Among the subgroup analysis triple negative patients and Her2 Only subgroup showed maximum complete response rates.

Lim et al [9] did analysis of response rates of different population presenting to five different hospitals in Singapore and Malaysia. Pathological complete response rates were 14.4%. pCR rate was the highest among women who had higher grade, smaller size, estrogen receptor negative, human epidermal growth factor receptor 2-positive disease. On subgroup analysis of the Indian population pCR rates drop down to 11.3%.

The difference in complete response rates could be further correlated by biomolecular classification of study group.

CONCLUSION:

Indian women with breast cancer are at least a decade younger than the western population. Most of the cases present at more advanced stage and responds less to chemotherapy. The difference in age stage and response appear to suggest different biology than its western counterparts. It appears that Indian breast cancer to more biologically more aggressive cousin. Further studies involving the molecular profiling of the study group would display a clearer picture regarding

the differences. Considering these differences, standard recommendations might be needed to be reevaluated to help tackle the breast cancer problem in Indian subcontinent.

REFERENCES:

1. Carol DeSantis, MPH1*; Jiemin Ma, PhD1; Leah Bryan, MPH1; Ahmedin Jemal, DVM, PhD2 Breast Cancer Statistics, 2013 CA: A Cancer Journal for Clinicians
2. SEER Cancer Statistics Factsheets: Female Breast Cancer. National Cancer Institute. Bethesda, MD, <http://seer.cancer.gov/statfacts/html/breast.html>
3. Ferlay J, Soerjomataram I, Ervik M, Dikshit R, Eser S, Mathers C, Rebelo M, Parkin DM, Forman D, Bray, F. GLOBOCAN 2012 v1.0, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 11 [Internet]. Lyon, France: International Agency for Research on Cancer; 2013
4. Adedayo A. Onitilo, MD, MSCR, FACP; Jessica M. Engel, MSN, FNP-BC; Robert T. Greenlee, PhD; and Bickol N. Mukesh, PhD Breast Cancer Subtypes Based on ER/PR and Her2 Expression: Comparison of Clinicopathologic Features and Survival Clinical Medicine & Research Volume 7, Number 1/2: 4-13
5. Suraj Manjunath & Jyothi S. Prabhu & Rohini Kaluve & Marjorie Correa & T. S. Sridhar Estrogen Receptor Negative Breast Cancer in India: Do We Really Have Higher Burden of this Subtype?
6. Madhuri Kakarala*1,2, Laura Rozek3, Michele Cote3, Samadhi Liyanage1 and Dean E Brenner1,2,4 histology and receptor status characterization in Asian Indian and Pakistani women in the U.S. - a SEER analysis BMC Cancer 2010, 10:191
7. Rohit Bhargava, MD1; Sushil Beriwal, MD2; David J. Dabbs, MD1; Umut Ozbek, MS3; Atilla Soran, MD4; Ronald R. Johnson, MD4; Adam M. Brufsky, MD5; Barry C. Lembersky, MD5; and Gretchen M. Ahrendt, MD4 Immunohistochemical Surrogate Markers of Breast Cancer Molecular Classes Predicts Response to Neoadjuvant Chemotherapy A Single Institutional Experience With 359 Cases
8. Roman Rouzier,1,4 Charles M. Perou,5 W. Fraser Symmans,2 Nuhad Ibrahim,1 Massimo Cristofanilli,1 Keith Anderson,3 Kenneth R. Hess,3 James Stec,6,7 Mark Ayers,6 Peter Wagner,1 Paolo Morandi,1 Chang Fan,5 Islam Rabiul,1 Jeffrey S. Ross,6 Gabriel N. Hortobagyi,1 and Lajos Pusztai1 Breast Cancer Molecular Subtypes Respond Differently to Preoperative Chemotherapy Clin Cancer Res 2005;11(16) August 15, 2005
9. Li Yan Lim1,*; Hui Miao2,*; Joline S. J. Lim3; Soo Chin Lee3; Nirmala Bhoo-Pathy4; Cheng Har Yip5; Nur Aishah B. M. Taib5; Patrick Chan6; Ern Yu Tan6; Swee Ho Lim7; Geok Hoon Lim7; Evan Woo7; Yia Swam Tan7; Jung Ah Lee7; Mabel Wong8; Puay Hoon Tan9; Kong Wee Ong10; Fuh Yong Wong11; Yoon Sim Yap7,8 & Mikael Hartman2,12 Outcome after neoadjuvant chemotherapy in Asian breast cancer patients