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EPIDEMIOLOGICAL INDICATORS AND PREDISPOSING FACTORS AMONG PATIENTS OF BREAST CANCER IN NORTHERN INDIA: AN INSTITUTIONAL STUDY

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ABSTRACT

Background: Breast cancer is the most commonly diagnosed cancer with highest mortality. It has different prognosis in Indian scenario with aggressive presentation as compared to the western population. This study was thus done to study the epidemiology and highlight these differences in clinical and prognostic factors. **Materials and Method:** This retrospective study was conducted to collect data on histologically proven cases of breast cancer from June 2017 to December 2019. Data pertaining to socio demographic factors, tumor factors, hormone receptor positivity and human epidermal growth factor receptor type 2 (HER2) were collected. Data was thus interpreted as frequency tables and graphs. **Results:** A total of 455 patients were registered in this time period. Patients presented at an early age group of 31-50 years accounting for 53.6% of patients and at a higher stage of stage III accounting for 48.5% of patients, which is in contrast to the western population. 1.5% patients were of male gender. 57.6% of patients presented with lump in left breast and upper outer quadrant was most commonly involved in 36.1% of patients. Estrogen receptor positivity was seen in 45.5% patients and HER-2/neu was positive in 35.9%. **Conclusion:** Lower age of presentation, higher stage at the time of presentation, lower rate of positivity in ER and slightly higher expression of HER-2/neu receptors, point towards aggressive nature of breast cancer in Indian population as compared to various studies done in western countries. Subject Area: ONCOLOGY
Keywords: Breast Cancer, Age, Stage, ER, HER-2/neu

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INTRODUCTION

According to GLOBOCON 2020, for the first time, female breast cancer has become the leading cause of global cancer incidence worldwidewith almost 2.3 million new cases (11.7% of allcancer cases) closely surpassing lung cancer (11.4% of all cancer cases).

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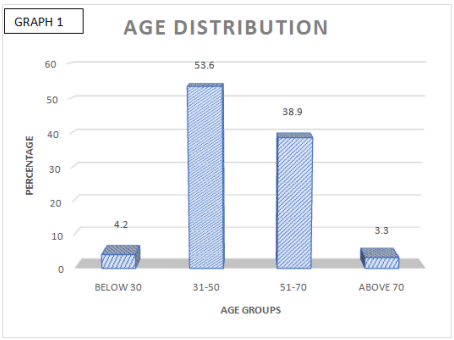
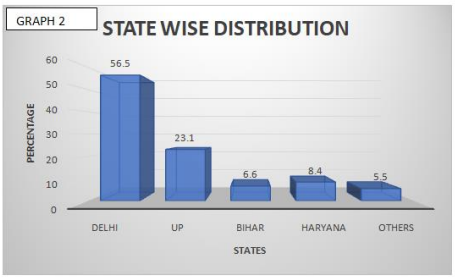
And this is particularly dueto its high prevalence in low and middle-income group countries. In India also, breast cancer is the leading cause in terms of incidence (13.5% of total cases) and mortality (10.6% of total cases) followed by cancer lip and oral cavity.1 In most of the cases risk factors like age, parity, stage at presentation, genetics, hormone factors, smoking, associated comorbidities, environment and demography play an important role. 2There is a significant difference in epidemiological profile of breast cancer in Indian women as opposed to western countries women.3Indian women tend to have a younger, pre-menopausal age at presentation peaking between 40-50 years as compared to the western countries

females.4 Furthermore, more than 50% of patients in United States present in stage I breast carcinoma, which is contrastingly different in Indian scenario where almost 50% patients present in stage III.5This is attributed due to various reasons such as obstacles to health services, low socioeconomic status, unawareness and insufficiency of screening programmes.6 So is true for the mortality associated with breast cancer, which is declining in western countries but increasing in India.5 Breast cancer treatment comprises of surgery, anticancer chemotherapy, radiation therapy and hormonal therapy and immunotherapy.7





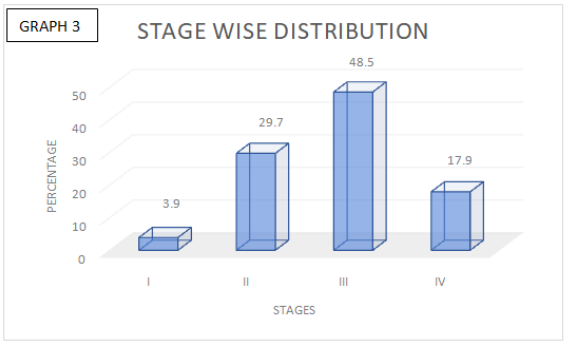
The hormonal receptor status, and human epidermal growth factor receptor type 2 (HER2) are not only used as predictive markers for identification of high-risk phenotype but also for selection of adequate therapies.8 In this study, we will discuss theincidence and trends of breast cancer and will also determine the status of receptors, stage and othermorphological prognostic parameters in population registered in an institute in NEW DELHI, INDIA.

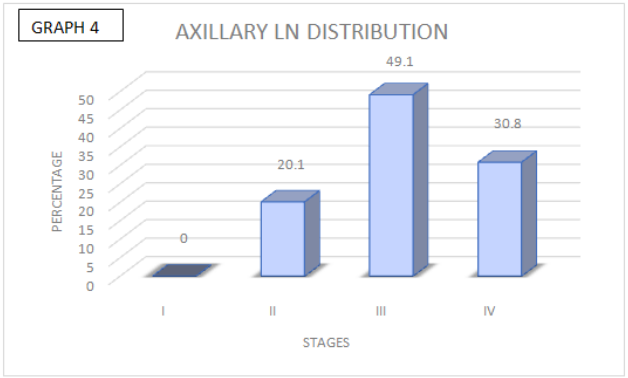
METHOD AND MATERIAL

A retrospective study of carcinoma breast patientsregistered in department of Radiation Oncology, Safdarjung Hospital New DELHI, was conducted. Data was collected from departmental records for the time duration of June 2017 to December 2019. All the patients were either biopsy proven or postoperative (MODIFIED RADICAL MASTECTOMY, LUMPECTOMY WITH AXILLARY CLEARANCE, TOILET MASTECTOMY) at the time of registration. All patients were staged according to the TNM classification by The American Joint Committee on Cancer (AJCC) 8th edition for breast carcinoma. Data was collected based on socio-demographic profile (such as age, gender, region, co-morbidities, family history), tumor profile (site wise distribution of lump, histo pathological type, presence or absence of axillary and supraclavicular lymph nodes, hormonal status) along with the treatment received. We also collected data for expression of ER (estrogen receptor), PR (progesterone receptor) and Her-2/neu in the breast cancer tissue specimens. In case of equivocal findings of HER-2/neu, FISH (fluorescence in situ hybridization) test had been conducted as per departmental protocol. Data was collected, analyzed and presented as frequency tables and figures.

RESULTS

A total of 455 patients were included in this study. Table 1 demonstrates the patient and tumor characteristics of this study. The peak of breast carcinoma was seen in the age group 31-50years with 244(53.6%) patients followed by 51-70 years with177 (38.9%) patients (GRAPH 1). Male patients also presented with breast carcinoma accounting for 7 (1.5%) patents in total. Since our hospital is a tertiary care center situated in New Delhi, apart from New Delhi(56.5%), patients also reported from adjoining states like Uttar Pradesh(23.1%), Haryana (8.4%) and Bihar (6.6%).(GRAPH 2). No substance abuse was reported by 86.4% of patients while the remaining usually used to either smoke cigarette or chew tobacco. Most common co-morbidity seen in our patients was Diabetes Mellitus accounting for 69 (15.2%) patients while majority of the patients (61.9%) did not have any co-morbidities. Positive family history was found in 33 (7.2%) of patients with 6.1% of them being first degree relatives and 1.1% were second degree relative. Left breast was most commonly involved in 262 (57.6%) patients, with upper outer quadrant being the most common site in 164 (36.1%) patients. Lymph nodal involvement was also commonly seen in our study, wherein axillary lymph nodes were positive in 299 (65.7%) patients while, supraclavicular lymph nodes were seen in 69 (15.2%) patients. Patients were most commonly diagnosed in third stage accounting for221(48.5%) patients, followed by stage II, IV and I with 135 (29.7%), 81 (17.9%) and 18 (3.9%) patients respectively.(GRAPH 3). If we see the stage wise distribution of axillary lymph nodes, out of 299 patients, 60(20.1%) patients had positive nodes in stage II, 147(49.1%) in stage III and 92(30.8%) in stage IV (Graph 4). Supraclavicular nodes on the other hand were only seen in stage III (24.6%) and stage IV (75.4%).





Infiltrating ductal carcinoma (IDC) was the most common histological type evaluated, attributing to approximately394(86.5%) cases. Out of these, grade 2 was reported most number of times accounting for 237 (52.1%) cases. Other histopathologies documented were Medullary Carcinoma, DCIS, Carcinosarcoma, Phylloides tumor and Pagets disease. Estrogen receptor positivity was seen in 209 (45.5%) patients and HER-2/neu positivity in 170 (35.9%) patients. All the three receptors were positive in 36 (8.7%) patients and triple negative disease was seen in 120 (29.1%) cases.

Table 1 Patient and tumor characteristics

CHARACTERISTICS	Number (%)
Age distribution	
<30years	19 (4.2%)
31-50 years	244 (53.6%)
51-70 years	177 (38.9%)
>71 years	15 (3.3%)
Gender	
Female	448 (98.5%)
Male	7 (1.5%)
State wise distribution	
Delhi	257 (56.5%)
Uttar Pradesh	105 (23.1%)
Haryana	38 (8.4%)
Bihar	30 (6.6%)
Others	25 (5.5%)
Co-morbidities	
None	282 (61.9%)
Diabetes Mellitus	69 (15.2%)
Hypertension	43 (9.5%)
Thyroid Dysfunction	34 (7.5%)
Others	27 (5.9%)
Family History	
None	92.8%
First degree relative	6.1%
Second degree relative	1.1%
Presenting complaints	
Breast lump	248 (54.5%)
Nipple Retraction	19 (4.1%)
Nipple discharge	17 (3.8%)
Old treated Ca breast	171 (37.5%)
Duration of symptoms	
<3 months	98 (21.5%)
3 to 6 months	129 (28.4%)
6months to 1 year	144 (31.7%)
> 1 year	84 (18.4%)
Laterality	
Left	262 (57.6%)
Right	193 (42.4%)
Distribution of lump	
Upper outer quadrant	164 (36.1%)
Upper inner quadrant	59 (12.9%)
Lower outer quadrant	44 (9.6%)
Lower inner quadrant	38 (8.4%)
Central	73 (16.1%)
Whole breast	77 (16.9%)
Axillary Lymph Node	
Present	299 (65.7%)
Absent	156 (34.3%)
Supraclavicular Lymph Node	
Present	69 (15.2%)
Absent	386 (84.8%)
Histopathology Type	
IDC grade 1	32 (7.1%)
IDC grade 2	237 (52.1%)
IDC grade 3	125 (27.5%)
Invasive carcinoma	21 (4.7%)
Phylloidstumor	15 (3.3%)
DCIS,	12 (2.6%)
Medullary carcinoma,	6 (1.3%)
Carcinosarcoma	4 (0.8%)
Paget disease	3 (0.6%)
Hormonal and HER2neu status	
ER positive	209 (45.5%)
PR positive	183 (39.2%)
HER 2 neu	170 (35.9%)
ER/PR positive	143 (34.7%)
Triple positive	36 (8.7%)
Triple negative	120 (29.1%)
Stage	
Stage I	18 (3.9%)
Stage II	135 (29.7%)
Stage III	221 (48.5%)
Stage IV	81 (17.9%)
Compliance	
Regular F/U and CR	136 (29.8%)
Regular F/U and PD	64 (14.1%)
Lost to F/U	255 (56.1%)

IDC: Infiltrating ductal carcinoma, DCIS: ductal carcinoma in situ, ER: Estrogen receptor, PR: Progesterone receptor, HER 2 neu: Human epidermal growth factor, F/U: Follow up, CR: complete response, PD: Progressive disease

Compliance in our patients was very poor and 56.1% patients lost to follow up. Of the remaining 43.9% patients, 29.8% patients were on regular follow up and had complete response while 14.1% patients were on regular follow up and had progressive disease (Graph 5). Almost 40% of the total number of patients completed the scheduled radical treatment.

DISCUSSION

Breast cancer is the most common cancer diagnosed in the world as well as in India.1 Though the mortality in western countries is showing declining trend, in India the mortality is still on rise. This can partly be attributed to better screening programs, diagnosis at an early stage and awareness for breast cancer in the western population.1,9Due to lack of the above factors, almost 50% of our patients presented in third stage while only 33.6% patients were diagnosed in stage I and II.

Significant number of our patients (>50%) were diagnosed at an early age group of <50 years and mostly were premenopausal. The more worrying part is the fact that 19 patients presented in <30 years of age group. This trend of early age presentation, has been documented in other studies as well and may point towards poor survival in Indian population.10Presentation at younger age group is usually associated with aggressive disease, larger size of tumour and increased number of positive lymph nodes, which leads to overall poor prognosis and dismal survival in younger age group.11 Male breast cancer has usually been documented in 1% of all breast cancers and even though the diagnosis is delayed, not much difference in mortality is seen as compared to female counterparts.12,13 In our study also 1.5% of the total patients were of male gender.

Distinctive clinical features and cancer biology has been seen in left breast cancer patients compared to right. Studies, done previously have shown more cases of breast cancer on left side with ratio of left to right ranging from 1.05-1.26. In our study left sided breast was most commonly involved in 57.6% patients as compared to the right side and ratio of left to right was 1.35.14 The location of tumour within breast was found to have similar distribution as in other studies15,16, with upper outer quadrant being the most common site (36.1%) and lower inner quadrant being the least common site (8.4%). Few of the risk factors associated with breast cancer include substance abuse, positive family history and associated co-morbidities. Paksresht et al. had reported less than five percent of women had a history of smoking or alcohol consumption.[17] But in our study we found history of addictions in approximately 13% of the patients. This can be attributed to increased prevalence of smoking and tobacco chewing among the lower socio-economic and uneducated women, which constituted majority of our population.[18]Our study reported incidence of family history to be around 7.2%, which is similar to a study done by Agarwal etal, with 5% family history.[19]Presence of co-morbidities influence the preferences for treatment and treatment outcomes leading to less aggressive treatment with chances of poor treatment outcome.[20] In our study Diabetes Mellitus was the most common co-morbidity accounting for

15.2% of cases followed by hypertension. Previous malignancy was also reported in 0.2% of patients in our study. Positive ER/PR status usually correlates with better survival and is considered as a good prognostic marker.[21] In our study we documented 45.5% positivity rate for ER and 39.2% for PR. This is lower than the prevalence of receptor positive breast cancer in western studies, where they have reported 70-80%ER expression and 60-70% PR expression.[22,23] Though in other Indian studies also the receptor positive expression has been found to be similar to our study.[21]

On the other handHER-2/neubreast cancers usually have different natural history and dismal prognosis. In our study we found 35.9% of the patients to be HER-2/neu positive which is similar to 39.8% positivity reported by Singh et al.[24] This is slightly higher than the 25-30%positivity rate documented in western studies.[25] This high rate of HER-2/neu positivity while low rate of ER positivity is again pointing towards the aggressive nature of disease in our country. The compliance to follow up was very poor in our study where in 255 patients were lost to follow up after completion of treatment. There are various reasons for this in Indian scenario which is predominantly a patriarchal society with general indifference towards the health of females, ignorance of the women towards their own health due illiteracy and various social taboos and myths widely present in lower socioeconomic class.[19] In conclusion, various clinical, pathological and prognostic differences in breast cancer between the western and Indian population warrants, more aggressive treatment in Indian population and fresh studies should be undertaken keeping this in mind.

CONCLUSION

Lower age of presentation, higher stage at the time of presentation, lower rate of positivity in ER and slightly higher expression of HER-2/neu receptors, point towards aggressive nature of breast cancer in Indian population as compared to various studies done in western countries. Various clinical, pathological and prognostic differences in breast cancer between the western and Indian population warrants, more aggressive treatment in Indian population and fresh studies should be undertaken keeping this in mind.

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