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Clinical Profile and Treatment Outcome of Carcinoma Breast Patients---Experience From A Tertiary Care Hospital of Western Up

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ABSTRACT

The epidemiological data, management strategies and treatment outcomes for carcinoma breast patients were analyzed in patients admitted to a tertiary care hospital of western up. Hospital records of 399 patients admitted for over a period of five years (January 2011 to December 2015) were used for data analysis. The maximum no. of pts presented was of 40-49 yrs age group (41.35%).66.6% pts were postmenopausal. The most common complaint was painless lump. Most of the patients (48.62%) presented to clinician after 1 yr of developing symptoms and only 5.51% pts within 3 months of onset of symptoms. 68.41% pts presented as post op cases including residual and recurrent disease while 29.32% pts presented as locally advanced breast cancer. Familial breast cancer was very uncommon. Left sided breast cancer was slightly preponderant. The most common histology was infiltrating duct carcinoma.38.23% pts received adjuvant radiotherapy after receiving adjuvant chemotherapy.16.99% pts lost to follow up after completion of treatment. The 2yr DFS in the 3 arms (25#,20#,17#) was 44.68%,51.61% and 50% respectively, while 2 yrs overall survival was 61.7%,51.61% and 75% respectively. Loco-regional failures were seen in 0%, 3.22% and 12.5% cases and distal recurrence in 27.65%, 9.67% and 12.5 consecutively. While 5yrs overall survival in 25# vs. 20# arm was 9.7% vs. 4%. Mean age of presentation was found to be lower compared to the western world, with an average one decade before as mentioned in literature. Most of the patients were not having any risk factors except being female. Most of the patients got defaulted in view of long waiting list for radiotherapy so we are trying to switchover conventional protocol to hypo-fractionated Radiotherapy protocol so more no. of pts can be benefitted particularly in a government setup.

Keywords: Breast cancer, risk factors, clinical profile, hypo fractionation Radiotherapy

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INTRODUCTION

Breast cancer in female is a major medical problem. World wide it is the most common form of cancer in females, affecting at some time in their lives approximately one out of nine to thirteen women who reach age ninety in the western world. Presently, 75,000 new cases occur in India each year[1] .The incidence of breast cancer is raising steadily over time. This seems to be closely related to industrial development and changing life style. In India it is the second most common cancer after cervix accounting for 19% of the total cancer burden[2]

The disease is higher in urban areas rather than rural areas, with Delhi having the highest incidence in the country followed by Mumbai, Chennai and Bangalore[3]. The risk of breast cancer increase with age. In the west only < 1 % cases are seen in women less than 30 years, about 6 – 7% in between 30 – 40 years. This disease is more common in women with better socio economic status due to unknown reasons but life style differences and dietary habits are said to be risk factors. The relative risk of carcinoma breast is 1.7 in a woman who has an immediate relative i.e. mother, daughter or sister having this problem. If these relatives have got the disease onset in pre-menopausal age, the risk is increased three folds while it is 1.5 if the onset is in post-menopausal age. The lifelong exposure to female reproductive hormones is known to be associated with increased risk of breast cancer. Similarly there has been known association between plasma estrogen levels & breast cancer.

Women having one full term pregnancy have a 25% decrease in the risk of breast cancer in contrast to nulliparous females. There is also evidence that women having more children are more protected against breast cancer. Longer duration of lactation also reduces the breast cancer incidence.[4,5] It was supposed for long that the breast cancer risk increases with high intake of dietary fat. There may be a protective effect of vegetables intake .In a study by American Cancer Society the risk of mortality due to Ca breast was significantly increased due to obesity. Physical exercise may reduce breast cancer risk. This reduction has been seen both in pre & post menopausal women. Breast cancer is more common on the left side as compared to right due to unknown reasons. It is most common in upper outer quadrant followed by central area, upper inner, lower outer & lower inner quadrants. The usual presentation is with a painless lump in the breast, but there are many differences between the presentations of breast cancer in developed and under developed areas in the world. It is not common to see large tumors with skin ulcerations, bleeding and peau'd orange presentation in the countries with good socio economic status, while it is a common finding in the poor countries. Similarly it is a routine to pick up very early suspicious lesions in the developed countries where screening mammography are carried out effectively.

Multivariate analysis have shown that a longer duration of symptoms had a highly significant adverse effect on survival.[6] The presence of hormone receptors on the tumor tissue predicts the benefit a patient can get from hormone treatment. HER-2 positive tumours are generally related with comparatively poor prognosis than HER-2 negative tumours. Mastectomy is the most common procedure carried out in most of the parts in India .As most of the patient present after mastectomy with or without axillary clearance. If axillary clearance is there it is usually incomplete so keeping all the points in view all pts receive adjuvant loco-regional radiotherapy to chest wall ,axilla and supraclavicular region and in few cases internal mammary chain also in our set up. The conventional dose is 5000cGy in 5wks @2Gy per fraction and is widely acceptable protocol. Due to increase in incidence of breast cancer and long waiting list for radiotherapy we are trying to switch over this conventional protocol into hypo- fractionation protocol .A hypo fractionated protocol means reducing no of fractions and overall treatment time while increasing dose per fraction. At Christie Hospital Manchester there has been a routine to deliver 5000 -5500 CGy in 15-16 fractions for most of the tumors for decades & they have shown equivalent results in most of the settings. For breast cancer they use 4000 CGy in 3 weeks i.e. 15 fractions with good results.

Carcinoma breast continues to be the focus of intense basic and clinical research. Hence, this retrospective study was carried out to know the epidemiology, clinical presentation, risk factors and management strategies for breast patients in a tertiary government setup.

MATERIALS AND METHOD:

A total of 467 primary breast cancer patients were registered in the department over a five-year period (January 2011 - December 2015) out of which 399 patients were admitted for the treatment and were taken up for study. A detailed analysis of patients was done according to a planned proforma. The required information was collected from the medical records of the patients submitted in the department. Radiotherapy was delivered by Co^{60} teletherapy machine by 3 field/4field techniques.

In this study we have tried to represent the clinical profile of breast cancer pts in terms of patient characteristics, tumor characteristics, duration of symptoms, and way of presentation and pattern of treatment received, treatment outcome and follow up pattern in a tertiary government setup.

The purpose of this study was to see the epidemiological pattern, presentation pattern of ca Breast patients, treatment outcome of different radiotherapy fractionations practiced in the department in terms of loco-regional recurrence, distant recurrence, 2 yr overall survival, Disease free survival,5yr overall survival and to search out the cause of defaulter of pts from treatment.

RESULTS AND DISCUSSION

Out of 467 patients registered in the department, 399 pts were evaluable for the study that means only 85.43% pts received treatment after enrolment. The maximum no. of pts presented was of 40-49 yrs age group (41.35%) while 2nd decade pts were 3.5%. 66.6% pts were postmenopausal.

The most common complaint was painless lump in the breast. Most of the patients (48.62%) presented to clinician after 1 yr of developing symptoms and only 5.51% pts presented within 3 mths of onset of symptoms.62.15% pts were from rural area of local place.65.65% patients were having 2 or more para.

Left side lesions were more common than Rt side lesions (52.3% vs 46.86%).Maximum no. of pts were of stage III (64.39%). In most of the pts (76.19%) receptor status were not known. In pts whom receptor status was known, triple negative pts were 23.95% while triple positive were 16.66 %.

(Table-1)

68.41% pts presented as post-op cases, out of which 16.03% pts were with post-op residual/recurrent disease while 29.32% pts presented as locally advanced disease.

Only 36.09% pts received Neo-adjuvant chemotherapy while 55.13% pts received adjuvant chemotherapy.(Table-2)

Out of 399 pts, only 153 pts (38.34%) received radiotherapy in the dept. out of which 88.88% received radical radiotherapy while 7.18% pts received palliative radiotherapy.62.49%pts could get radiotherapy after 6 months of surgery due to long waiting list for radiotherapy.

Adjuvant radiotherapy received as per 25#, 20#, 17# and 15# protocol by 42.64%, 33.08%, 12.5% and 11.76% pts respectively. (TABLE-3)

AS 15# protocol pts completed only 1 yr of follow up so this arm was not included in 2 yr survival analysis. The 2yr DFS in the 3 arms(25#,20# and17#) was 44.68%,51.61% and 50% respectively while 2 yrs overall survival was 61.7%,51.61% and 75% respectively.. Loco-regional failure are seen in 0%,3.22% and 12.5% cases while distal recurrence in 27.65%,9.67% and 12.5% pts respectively.

While comparing 5yrs overall survival it is 9.7% vs. 4 %.(25# vs. 20#)

TABLE-4)

Table 1: Patient's characteristics

Age(yrs)	No of pts	%
20-29	14	3.50%
30-39	50	12.53%
40-49	165	41.35%
50-59	102	25.56%

60-69	50	12.53%
70-79	17	4.26%
=/>80	1	0.25%
Premenopausal	133	33.33%
postmenopausal	266	66.66%
Local place	248	62.15%
Nearby districts	127	31.83%
Remote area	24	6.01%
=/< 2	78	19.54%
>2-4	161	40.35%
>4	101	25.3%
nullipara	59	14.7%
Rt side lesion	187	46.86%
Lt side lesion	209	52.3%
B/L	3	0.75%
Presentation		
Lump	321	80.45%
Lump with pain	68	17.04%
Lump with pain and d/s	10	2.5%
Duration of symptoms		
<3mth	22	5.51%
3-5mth	63	15.78%
6-8mth	79	19.79%
9-11mth	41	10.27%
>12mth	194	48.62%

Table 2: Disease presentation

As per presentation		
Postop NED	209	52.38%
POSTOP residual	36	9.52%
Postop recurrence	26	6.51%
LABC	117	29.32%
Metastatic	11	2.75%
As per staging		
Stage I	7	2.04%
STAGE IIA	44	12.8%
STAGE IIB	61	17.7%
STAGE IIIA	80	23.32%
STAGE IIIB	115	33.52%
STAGE III C	26	7.55%
STAGE IV	10	2.91%
NA	56	14.03%
Receptor Status		
unknown RECEPTOR status	304	76.19%
known receptor status	96	24.06%
ER/PR/HER+ve	16	16.66%
ER/PR/HER –ve	23	23.95%
ER/PR+ve	11	11.45%
ER/PR-ve	6	6.2%
Er+ve/Pr-ve	14	14.54%
Er-ve/Pr+ve	4	4.16%
ER+/Pr+/HER-	11	11.45%
ER-/PR-/HER+	10	10.4%

Table-3: As per Treatment Received

Chemotherapy		
NACT Received	144	36.09%
Adjuvant CT Received	220	55.13%
Radiotherapy		
Palliative	27	17.64%%
Radical +Palliative Both	11	
Radical RT(adjuvant)	136	88.88%
50Gy/25#	58	42.64%
45Gy/20#	45	33.08%
4250CGY/17#	17	12.5%
40GY/15#	16	11.76%
GAP between Sx and RT		
<3mth	7	5.16%
3-6mth	52	38.23%
7-9mth	44	32.35%
>9mth	41	30.14%

Table 4: End points results after deducting lost to follow-up pts

Fractionations	No of pts(enrolled)	Evaluable pts	1yr DFS	2yrDFS	Iyr OS	2yr OS	Loco-regional recurrence	Distant recurrence	Death	3yr os	5yros
25#	57	47	32 (68.08%)	21 (44.68%)	45 (95.74%)	29 (61.7%)	0 (0%)	13 (27.65%)	1 (2.12%)	13/41 (31.7%)	4/41 (9.75%)
20#	45	31	26 (83.87%)	16 (51.61%)	31 (100%)	16 (51.61%)	1 (3.22%)	3 (9.67%)	1 (3.22%)	10/25 (40%)	1 (4%)
17#	17	16	13 (81.25%)	8 (50%)	16 (100%)	12 (75%)	2 (12.5%)	2 (12.5%)	0	7/14 (50%)	0
15#	15	14	11 (78.57%)	-	14 (100%)	-	0 (0%)	3 (21.42%)	0	0	0

The purpose of this analysis was to study the clinical profile of breast cancer patients at a tertiary care hospital in western UP. The maximum no. of pts presented was of 40-49 yrs age group (41.35%) as also reported in studies from India and other Asian countries[1,7,8] and this is one decade earlier than western countries where carcinoma is predominantly seen in the fifth and sixth decade[9,10,11,12]. Out of the entire patient, 62.15 % were from rural area of local district. However, other reports from India as well as western world show higher incidence in urban population compared to the rural population[4,12]. The difference may be due to lack of health facilities in the villages. The other aspect may be being a government setup most patients attending the hospital belong to rural background due to economic constrains. Furthermore, the consolidated report of the Indian Council of Medical Research (ICMR) on Population Based Cancer Registry (PBCR) cites that 70 - 80% of India's population resides in rural areas and the currently available data is mainly from the urban registries, therefore, to estimate the load of cancer is difficult.[6]Painless **lump** in the breast was the chief presenting complaint in a majority of the patients (80.45%), as also reported in various studies[13,14], while 2.5% pts presented with complaints of lump with discharge.

Most of the patients (48.62%) presented to clinician after 1 yr of developing symptoms and this pattern shows that pt usually not present until symptoms become very stressful to the pts. This is because of lack of public awareness and negligence regarding their health. The left breast carcinoma incidence was more than right side collaborating with the previous reports[15,16,17,18].. Only 14.7% of the patients were nulliparous, whereas, 65.6% patients were with more than 2 children. However, other reports indicate higher incidence of breast carcinoma in nulliparous females [3,20,21], Incidence of breast carcinoma was more in postmenopausal (66.6%) patients. The earlier published reports also show that the risk of breast carcinoma increases with increasing age of menopau, possibly because the women are exposed to hormones for a longer duration.[22,23,24] Maximum no. of (64.39%) patients presented in Stage III disease in accordance with other reports from India..76.19% patients were not able to afford expenses of Receptor studies. Receptor status was known in only 24.06% patients, out of which triple negative pts were maximum i.e. 23.95%.

Most of the patient presented to us as post-op cases. Apprx 16.03% patients presented with either post-op residual disease or recurrent disease. Neoadjuvant chemotherapy was received by 36.09% pts and most of the pts were given FEC/FAC regimen .

Apprx 55.13% patients received adjuvant chemotherapy in the department. Only 38.34% patients turned up for Radiotherapy treatment out of which 88.88% patients received adjuvant loco-regional radiotherapy as per departmental protocol. The cause of defaulter of most of patients from radiotherapy may be the long waiting list due to resource insufficiency as per

patients load as most of the pts (62.49%) could get radiotherapy after 6 months of surgery. Conventional breast and/or chest wall irradiation uses 2 Gy daily fraction, for 5-6 weeks. Such a long treatment schedule has major implications on both patient quality of life and Radiotherapy departments[2,3] Some investigators have hypothesized that breast cancer is as sensitive as normal breast tissue to fraction size. According to the hypothesis, small fraction sizes of 2.0 Gy or less offer no therapeutic advantage, and a more effective strategy would be to deliver fewer, larger fractions that result in a lower total radiation dose [1]. This short (hypofractionated) RT schedule would be more convenient for patients,especially those coming from remote areas and for health care providers, as it would increase the turnover in Radiotherapy departments.

Keeping in mind the defaulter of pts and treating the patients with limited resources we have tried to switch over conventional radiotherapy (50Gy/25#/5wks) plan to hypo fractionation radiotherapy i.e. from 25# to 20# and 17# and now 15#. The 2yr DFS in the 3 arms (25#, 20# and17#) was 44.68%, 51.61% and 50% respectively, which is statistically comparable, while 2 yrs overall survival was 61.7%, 51.61% and 75% respectively. Loco-regional failure are seen in 0%,3.22% and 12.5% cases while distal recurrence in 27.65%,9.67% and 12.5% pts. While comparing 5yrs overall survival it is 9.7% vs. 4 %.(25# vs. 20#).1 yr disease survival results of 15# protocols are encouraging and rate of defaulter from radiotherapy is also reduced when compared to previous yrs.

CONCLUSION

The mean age of presentation for breast carcinoma is a decade earlier in our patients compared to patients from the west. Hence, mammography as a screening tool less sensitive due to higher density of breast tissue at younger age. Due to economic constrains most people are unable to afford mammography. Thus there is a need for developing other cost-effective screening modalities for breast cancer in addition to propagating breast self-examination in masses, for early detection. Hypo fractionation Radiotherapy may be a better option for a government set up where pts load is more. .

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