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PATTERNS OF FAILURE AND SURVIVAL IN ER/PR POSITIVE CARCINOMA BREAST WITH CONVENTIONAL VERSUS EXTENDED HORMONAL THERAPY.

Oncology/Radiotherapy

Dr. Girija Priya* Senior Resident, DRPGMC, Kangra, HP. *Corresponding Author
Dr. Anu Priya Senior Resident, GMC, Jammu (JKUT).
Dr Sushant Sharma DC/SMO, CAPF, MHA, GOI.

ABSTRACT

Breast cancer is the second most common cancer in the world. Globally over the last several decades, the incidence of breast cancer has increased and the greatest increase has been seen in Asian countries and women in their 40s are affected mostly. Adjuvant Endocrine therapy is highly effective and appropriate for nearly all women with Estrogen Receptor- and/or Progesterone positive tumors, making such treatment the most widely prescribed therapy for patients with cancer in both the developed and developing countries. The present study aimed to compare the pattern of failure and survival in Estrogen Receptor/Progesterone Receptor positive Carcinoma Breast with conventional i.e. patients who have received hormonal therapy for 5 years versus extended hormonal therapy i.e patients who have received hormonal therapy for more than 5 years. Assessing short & long term effects profile of these hormonal regime. The present retro-prospective study was conducted in a multidisciplinary Tertiary care hospital in Srinagar, over a period of 2 years (August 2016 to August 2018) and a total of 105 patients were included in the study. It was observed in the study that mean age of study participants was 46.5±8.55 years in group A, and 43.2±7.31 years in group B and majority (40.95%) of the participants were in the age group 40-49 years. In Group- A, 23 patients belonged to Urban and 28 belonged to Rural whereas in Group-B, 38 subjects belonged to Urban areas and 16 from rural area. It was concluded in the study that patients who are on extended hormonal therapy had overall high survival 5.71% in comparison to conventional therapy i.e., 1.96%.

KEYWORDS

Carcinoma, Breast cancer, Treatment, Estrogen, Progesterone, Failure, Success and Pattern.

INTRODUCTION

Breast cancer is the second most common cancer in the world. Globally over the last several decades, the incidence of breast cancer has increased and the greatest increase has been seen in Asian countries mostly women in their 40s are affected. [1,2]

Low survival rates in less developed countries were observed mainly due to the lack of early detection programmes, resulting in a high proportion of women presenting with late-stage disease, as well as by the lack of adequate diagnosis and treatment facilities.[2] Hormones have been associated with breast cancer especially Estrogens play a predominant role in the growth of breast cancer.[3]The Estrogen Receptor (ER), Progesterone Receptor (PR) profile of a female primary breast carcinoma plays a significant role as a predictive marker in patient management.

They also help in determining treatment options and subsequent patient response. Current therapeutic strategies for management of primary breast carcinomas rely on the accurate immune-histochemical (IHC) determination of hormone receptor status in order to determine the clinical utility of hormone-directed therapies such as Selective Estrogen Receptor Modulators (SERMs).[4]Adjuvant endocrine therapy is highly effective and appropriate for nearly all women with ER- and/or PgR-positive tumors, making such treatment the most widely prescribed therapy for patients with cancer in both the developed and developing world.[5]

Thus, the present study was undertaken to compare the pattern of failure and survival in ER/PR positive Carcinoma Breast with conventional i.e patients who have received hormonal therapy for 5 years versus extended hormonal therapy i.e patients who have received hormonal therapy for more than 5 years, along with assessing short & long term effects profile of these hormonal regime.

Aims and Objectives

1. To compare the pattern of failure and survival in ER/PR positive Carcinoma Breast with conventional versus extended hormonal therapy.
2. To study the short and long term side effect profile of these hormonal regime.

MATERIAL AND METHODS

The present retro-prospective study was conducted in a multidisciplinary Tertiary care hospital in Srinagar, over a period of 2 years (August 2016 to August 2018) after obtaining ethical permission from the institution.

A total of 105 patients with histologically confirmed CA Breast with ER/PR positive status who were registered at Regional Cancer Centre of Sher-I-Kashmir Institute of Medical Sciences Srinagar and categorized into 2 groups, group A had taken hormonal therapy for > 5 years and group B had taken hormonal therapy for < 5 years.

Inclusion Criteria:

1. Patients of carcinoma breast who were on hormonal therapy for at least 3- 5 years or more than 5 years.
2. Patients who were on regular follow up.

Exclusion Criteria:

1. ER, PR negative.
2. Patients who had not completed treatment.

Patients characteristics with regard to their age, presentation, laterality, investigations, hormonal receptor status, hormonal treatment prescribed and treatment received in each case were studied in detail. Follow up details were thoroughly studied with regard to loco regional failure, distant failure, overall survival and other comorbid conditions related to treatment. The response to treatment was assessed by clinico- radiological assessment.The data was recorded in Microsoft Excel sheet. Data was analysed with SPSS software version 16. Karl Pearson Chi-square test was done to determine the relationship between independent & dependent variable, Odd's ratio (OR) and their 95% confidence intervals (95% CI) were calculated and p value <0.05 is deemed statistically significant. Mean, Standard deviation, Standard error,95% confidence intervals were calculated.

RESULTS AND OBSERVATIONS

In the present study the mean age of study participants was 46.5±8.55 years in group A, and 43.2±7.31 years in group B and majority (40.95%) of the participants were in the age of 40-49 years. In group A 23 of the patients belonged to urban and 38 in group B. In group A 28 belonged to rural area and 16 in group B.

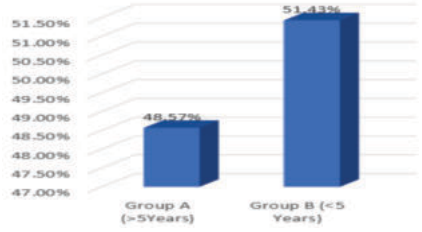

Figure 1. Duration of hormonal therapy

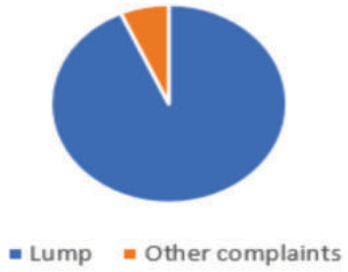

Figure 2. Chief complaints

Figure 1 and 2 depicted the distribution of patients according to duration of hormonal therapy and chief complaints. It was found that 51.43% had taken the hormonal therapy for less than 5 years and 48.57% had taken the treatment for more than 5 years. The majority of patients (93.33%) had lump in the breast as the chief complaint and 7(6.67%) had other complaint i.e lump, discharge from the nipple, swelling and pain.

Table 1. Comorbid conditions at the time of diagnosis

Groups	Hypertension	hypothyroid	None
Group A	7(13.72%)	3(5.88%)	41(80.40%)
Group B	9(20.1%)	1(1.90%)	41(78%)

Table 1 shows, that in Group A, 41 (80.40%) of the patients had no co-morbidity at the time of diagnosis and 41 (78%) in the Group B. 7 (13.72%) of the patients in the Group A had hypertension, and 3 (5.88%) had hypothyroid, 9 (20.1%) of the patients in the Group B had hypertension and 1 (1.90%) had hypothyroid at the time of diagnosis.

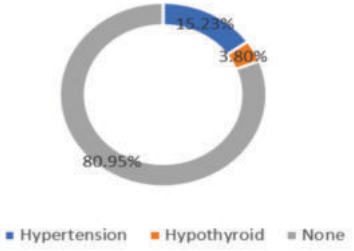

Figure 3. Comorbid conditions at presentation

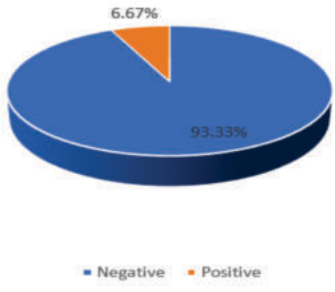

Figure 4. Family history

Figure 3 and 4 presented the comorbid condition at the time of presentation and family history of breast cancer. It was reported that 3.80% had hypothyroid, 15.23% had hypertension at the time of presentation and 6.67% (9.80% in group A and 3.70% in group B) patients had family history of breast cancer.

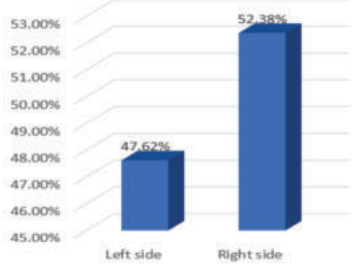

Figure 5. Laterality

It was reported that 52.38% (54.55% in Group A and 45.45% in Group B) patients had right side breast cancer and 47.62% (42% in Group A and 58% in Group B) patients had left side breast cancer as shown in figure 5.

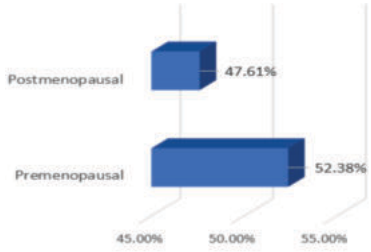

Figure 6. Menopausal status

Figure 6, show that 52.38% (49.02% in Group A and 55.6% in Group B) study participants were in premenopausal stage and 47.61% (50.98% in Group A and 44.4% in Group B) were in postmenopausal stage.

Table 2 Histopathological findings

Findings	Group A	Group B
Infiltrating ductal CA	39 (76.50%)	38 (70.40%)
Ductal cell CA	10 (19.6%)	10 (18.5%)
Infiltrating lobular CA	0	4 (7.40%)
Infiltrating papillary CA	0	1 (1.85%)
Medullary CA	1 (1.95%)	0
Mammary CA	1 (1.95%)	1 (1.85%)

In group A, 39 (76.5%) patients had histopathological variant of infiltrating ductal ca and 38 (70.40%) in group B as shown in table 2.

Table 3 Stage of disease

Stages	Group A	Group B
IA	12	13
IIA	10	16
IIB	12	11
IIIA	14	11
IIIB	0	2
IIIC	3	1

The different staging among the Group A and Group B were not significantly different statistically (p value 0.163). The patients on conventional therapy i.e. Group A had 10 (19.60%) of stage II A, Stage III A i.e. 14 (27.45%) and Stage III C i.e. 3 (5.88%) patients than the patients who were on extended therapy i.e Group B 16 (29.62%), 11 (20.3%) and 1(1.85%) respectively and among all the patients included in the study (105), highest number of the patients were in IIA as shown in table 3.

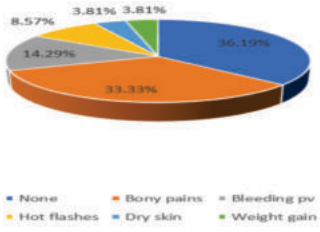

Figure 7. Side effects profile.

The Most common side effects identified among the patients were bony pains 35 (33.3% in Group A and Group B respectively) followed by bleeding per vaginum 15 (14.29% (9.8% in group A and 18.6% in group B)), hot flashes 9 (8.57% (11.8% in group A and 5.55% in Group B)), weight gain (7.84% in Group A) and dry skin (3.81% (1.96% in Group A and 5.55% in Group B)) as shown in figure 7.

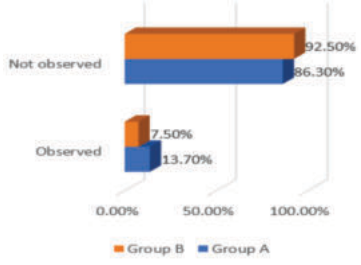

Figure 8. Locoregional failure (ipsilateral breast+ nodal failure)

The incidence of loco regional failure was not significantly different among both the both groups of patients (p value 0.29) as shown in figure 8.

Table 4 Multivariate analysis of locoregional recurrence

Term	Odds Ratio	95%	C.I.	Coeffic ient	S.E.	Z-Statistic	P-Value
STAGE	1.2	0.86	1.79	0.21	0.18	1.15	0.24
Status of menopause (premenopausal /postmenopausa l)	0.59	0.23	1.51	-0.51	0.47	-1.08	0.27

The logistic regression for the factors of locoregional failure showed no significant relation with the staging of carcinoma and menopausal status of the patients (P values 0.24 and 0.27 respectively) as presented in table 4.

Table 5 Distant failure

Distant failure	Group A	Group B
Opposite breast	1 (1.96%)	1 (1.85%)
Bone	7 (13.72%)	11 (20.45%)
Lung	1 (1.96%)	1 (1.85%)
Liver	1 (1.96%)	0
Brain	0	1 (1.85%)

Table 5 depicted that a total of 24 patients had distant failure. Number of the patients in which distant failure was not present were 81 (77.15%). In both the groups patients mostly had bone metastasis 18 (17.15%) as shown above. In Group- A, the number of the patients who did not had any distant metastasis were 41(80.40%) and in group B the no of patients were 40(74%). The number the patients who were having bone metastasis in Group A were 7(13.72%), and in Group B 11(20.45%). The number of patients who had metastasis in opposite breast were same in both the groups i.e 1(1.96%) in Group A ,1(1.85%) in Group B.

Table 6 Multivariate analysis of distant failure

Term	Odds Ratio	95%	C.I.	Coefficient	S.E.	Z-Statistic	P-Value
STAGE	0.96	0.53	1.74	-0.032	0.30	-0.10	0.91
Status of menopause (premenopausal/ postmenopausal)	0.51	0.11	2.29	-0.66	0.76	-0.87	0.38

The logistic regression for the factors of distant failure showed no significant relation with the staging of carcinoma and menopausal status of the patients (P values 0.91 and 0.38 respectively) as depicted in table 6.

Table 7 Overall Survival

Group	5 - 10	10 - 15	15 - <20	20 - <25
Group A	18 (35.29%)	23 (45.1%)	9 (17.65%)	1 (1.96%)
Group B	4 (7.40%)	34 (63%)	11 (20%)	5 (9.6%)

The survival of 20-25 years is significantly high among the patients in Group B 5(9.6%) compared to 1(1.96%) among patients in Group A (p value 0.003). The mean years of survival after starting of the therapy was 12.94 years in Group B compared to 11.64 years in Group A as shown in table 7. The survival was significantly high among the patients on extended therapy i.e. Group B.

DISCUSSION

In our study the mean age of both the groups was 40-50 years which correlates with the studies from India and Asian countries done by Sandhu et al, Chopra et al and Gupta et al.6,7,8

In our study 58.1% of the patients in both groups were from urban background as compared to rural background which correlates with western literature and Chopra et al.7

Lump in the breast was the chief presenting complaint in majority (93%) of our patients in both the groups as was reported by Raina et al, Sandhu et al and Arumugam Velappan et al. 8,6,9 In our study family history was positive in 6.6% of the patients in both the groups which correlates with the study done by Arumugam et al.9

In our study stage wise distribution of cases reflected that most patients were in stage III which is consistent with study done by Arumugam et al. and Nesa et al. in which 50% of the patients were in stage III.9,10

Our study showed infiltrating ductal carcinoma in 74% of the patients which correlates with the study done by Kakarala et al., Sunita Sexana et al. and Alwan et al.11,12,13

In our study the 55(52.38) % of the patients were premenopausal and 50 (47.62%) of the patients were postmenopausal in both the groups which correlates to study done by Bharadwaj et al.14

In our study we took ER positivity of >1% to consider a patient as ER positive. In our study the overall survival was significantly high among the patients on extended hormonal therapy ie 5.71% in comparison to conventional group i.e 1.96% which was significant. The most common side effects of hormonal therapy were bone pains i.e. 33.3% in both the groups which correlates with the study done by fatma et al. Second most common side effect was vaginal bleeding present in 14% of the patients. In patients in whom vaginal bleeding was present, those patients were shifted to letrozole, 5 in the group A and 10 in the group B. Tamoxifen was found to be associated with vaginal bleeding and endometrial thickness in The Arimidex, Tamoxifen Alone or in Combination (ATAC).15,16

In our study the locoregional failure was seen in 13% of the patients on conventional therapy i.e. Group A and 7.4% in the extended Group I.e. Group B correlates with ABCSG trial 6a in which patients who were disease free after 5 years of tamoxifen were randomly assigned to 3 years of anastrozole or no further treatment. With 62.3 months follow up the risk of locoregional recurrence reduced by 38% versus no further treatment. 17

In our study the incidence of locoregional failure among the group B i.e. who took extended therapy were marginally high which correlates with ATLAS trial which showed that 10 years of hormonal therapy further reduced the relapse risk by 30% and risk reduction of BC mortality of 48%.18

In our study distant failure was not present in 77.14% of the patients in both the groups which correlates with ATAC trial in which Distant recurrence rates also remained lower on anastrozole compared with tamoxifen in the hormone-receptor-positive subgroup throughout follow-up, with an absolute difference of 2·6% at 10 years.19

CONCLUSION

The present study concluded that patients who are on extended hormonal therapy had overall high survival 5.71% in comparison to conventional therapy i.e., 1.96%. Side effects, locoregional failure and distant failure was comparable in both the groups.

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