Original article:

A Comparative Study of Breast Cancer Prognosis in Premenopausal and Postmenopausal Women in Tertiary Care Hospital in Central India

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ABSTRACT:

Background: Worldwide breast cancer is the most common female cancer representing nearly 25% of all cancers. Prognosis of breast cancer patients depend on age of the patient, stage at diagnosis , hormonal status and treatment. **Objective:** This study was conducted to assess different types of histopathology and immunohistochemistry, management and prognosis in pre and postmenopausal breast cancer patients in a tertiary care center.

Methods: A hospital based retrospective observational study conducted on 100 breast cancer patients (divided into pre & post-menopausal groups) at Government Cancer Hospital, Indore, M.P., India in year 2016-17. Data was collected regarding clinical details, diagnostic tests, Histopathology and Immunohistochemistry examination, Staging and Management. Those patients were then kept on close follow-up for further 18 months to evaluate the probability of any local recurrence as well as distant metastasis.

Results: Maximum patients were between 41 to 50 year of age (31%). In Immunohistochemistry examination Luminal A subtype was most common (48% and 54%). Majority of patients were diagnosed with stage III in both groups (68% and 52%). Basal cell-like subtype was more prevalent in premenopausal breast cancer and had worst prognosis with 18% LR and 66% DM.

Conclusion: Delay in diagnosis may be due to rural background, poverty and lack of awareness. This study shows premenopausal breast cancer had a tendency to have larger tumor sizes, more positive lymph nodes, more negative hormone receptors and there was a relation between all of these features and more aggressive tumors and poorer prognosis.

Introduction:

Worldwide breast cancer is the most common female cancer representing nearly 25% of all cancers with an estimated 1.67 million new cancer cases diagnosed in 2012. Women from underdeveloped regions (883 000 cases) have slightly more number of cases compared to developed (794 000) regions.[1] During 2008–2012, India was facing challenging situation due to 11.54% increases in incidence and 13.82% increase in mortality due to breast cancer.[1,2] In India, majority of patients presented as locally advanced or at metastatic stage at the time of diagnosis. According to various studies, majority of carcinoma breast cases in the west report in stages I and II of disease, whereas in India 45.7% report in advanced stages.[3] Such conditions of Disease presentation along with unavailability of appropriate medical facilities results in increased mortality in India. Breast Cancers in the young tend to be more aggressive. Most of these cancers are HER2 positive and ER/PR negative, or HER2/ER/PR triple negative, and have a poor prognosis.The incidence of breast cancer increases steadily with age. Approximately 75% of all cases are diagnosed in postmenopausal women. The risk of developing breast cancer at age 25 years is 1 of

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19,608, whereas lifetime risk is 1 of 8 for women living into their 80s.[4,5] After menopause hormonal changes occur. So, in this study patients were divided into two groups premenopausal and postmenopausal. Management of breast cancer patients is based on age of the patient, stage at diagnosis, histopathological and immunohistochemistry findings. Hence, present study was conducted to assess different types of histopathology and immunohistochemistry, management and its complications, patterns of local recurrence and distant metastasis in pre and postmenopausal breast cancer patients in a tertiary care center.

Materials and Methods:

A tertiary care hospital based retrospective observational study was carried out to assess demography, histopathology, immunohistochemistry, management and prognosis of 100 post operated breast cancer women registered between January 2013 to December 2014 at Department of Radiotherapy, Government Cancer Hospital, MGMMC, Indore, M.P., India in year 2016-17. Patients were divided into two groups based on their menopausal status as premenopausal (group-A) and postmenopausal (group-B). Patients who had no menstrual flow since 12 months were considered as postmenopausal and the rest were considered as premenopausal. Patients who had natural menopause were only included in the study population. Detail data of the patient like name, age, site, diagnostic tests, HPE and IHC report, type of surgery, chemotherapy, radiotherapy, and hormonal therapy were recorded. Patient was evaluated regularly to access treatment response, treatment complications and were managed accordingly. Patient was kept on follow up for further 18 months to evaluate the probability of any local recurrence as well as distant metastasis in this duration. The two groups were later compared and evaluated regarding age at presentation, region, HPE, staging, hormonal status, management and its complications, treatment response, local recurrence and distal metastasis.

Results:

in the present study, age of patients of breast cancer were between 21 to 80 years; maximum (31) were between 41-50 year age group and minimum (3) were between 71-80 year group. In both groups of premenopausal and postmenopausal, left sided breast was affected more than right sided breast. In histopathological examination Invasive ductal carcinoma (ductal breast cancer) was maximum. It was 88% in premenopausal patients and 90% in postmenopausal patients. Invasive lobular carcinoma was 6% in premenopausal patients and 8% in postmenopausal patients. Medullary carcinoma and adenocarcinoma were in 0-4% cases. In Immunohistochemistry examination Luminal A was maximum. It was in 54% premenopausal and 48% postmenopausal patients. 'Basal like' was 32% in premenopausal and 20% in postmenopausal patients. 'HER 2+' was in 6% premenopausal and 16% in postmenopausal patients. 'Luminal B' was in 6% premenopausal and 16% in postmenopausal patients. According to the stage of breast cancer, maximum patients were of stage-III; 68% in premenopausal and 52% in postmenopausal group. In premenopausal group 28% patients were of stage-II and in postmenopausal group 46% patients were of stage-II. MRM Surgery was carried out in most of the patients of both groups (premenopausal-82% and postmenopausal-90%). In chemotherapy Anthracycline + Taxenes were given in 58% patients in group-A and Anthracycline was given in 62% group-B patients. 270cGy X 17# type of Radiotherapy was given in most of the patients. Local recurrence and distant metastasis rate was high in premenopausal (46%) as compare to postmenopausal breast cancer patients (26%). It is inferred that premenopausal breast cancer had a tendency to have

larger tumor sizes, more positive lymph nodes, more negative hormone receptors and there was a relation between all of these features and more aggressive tumors and poorer prognosis.

Table 1: Region and side wise distribution in pre & postmenopausal breast cancer patients

	Type	Premenopausal group (Group A)	%	Postmenopausal group (Group B)	%
Region	Rural	27	54%	29	58%
	Urban	23	46%	21	42%
Site	Right sided breast	22	44%	20	40%
	Left sided breast	28	56%	30	60%

Table -2 :HPE and IHC related distribution in pre & postmenopausal breast cancer patients

|	Type	Group-A	%	Group-B	%
HPE	IDC	44	88%	45	90%
	ILC	4	8%	3	6%
	MED CA	1	2%	2	4%
	ADENO CA	1	2%	0	0%
IHC	Luminal A	27	54%	24	48%
	Luminal B	3	6%	8	16%
	HER 2+	4	8%	8	16%
	Basal Like	16	32%	10	20%
Staging	I	2	4%	1	2%
	II	14	28%	23	46%
	III	34	68%	26	52%

Table -3: Distribution According To Type of Surgery, Chemotherapy, Radiotherapy and prognosis in Pre And Postmenopausal Breast Cancer Patients

Treatment & Prognosis	Types	Group A	Percentage	Group B	Percentage
Surgery	BCS	9	18%	5	10%
	MRM	41	82%	45	90%
Chemotherapy	Anthra + Taxenes	29	58%	18	36%
	Anthracyclines	21	42%	31	62%

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	Herceptine	0	0%	1	2%
Radiotherapy	NO RT	6	12%	4	8%
	300cGy X 13#	15	30%	13	26%
	270cGy X 17#	26	52%	25	50%
	610cGy X 5#	3	6%	8	16%
Prognosis	DFS	27	54%	37	74%
	LR	5	10%	3	6%
	DM	18	36%	10	20%
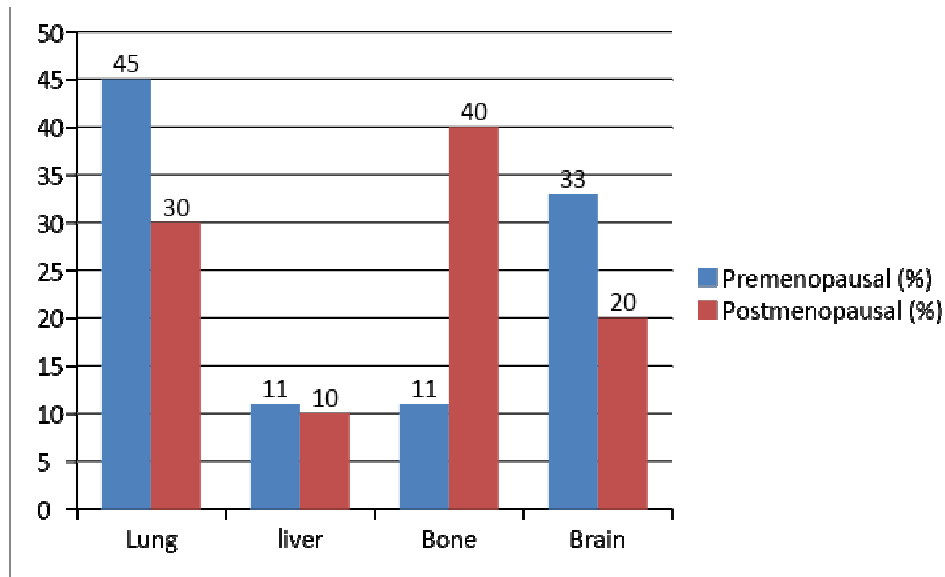
Graph 1: Comparison of Sites of Distant Metastasis In Premenopausal and Postmenopausal Breast Cancer Patients
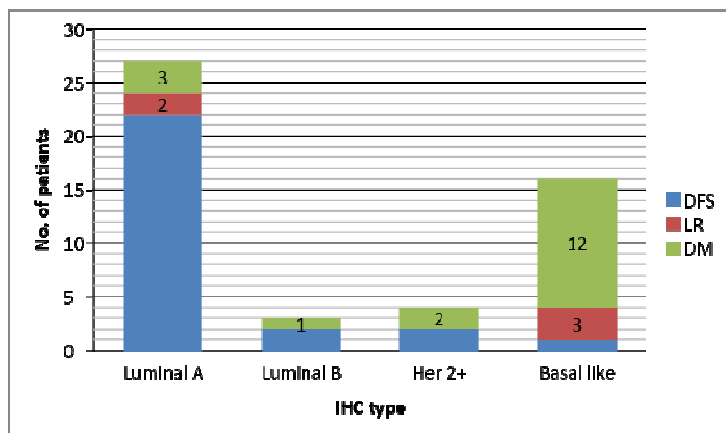
Graph 2: IHC Related Prognosis In Premenopausal Breast Cancer Patients
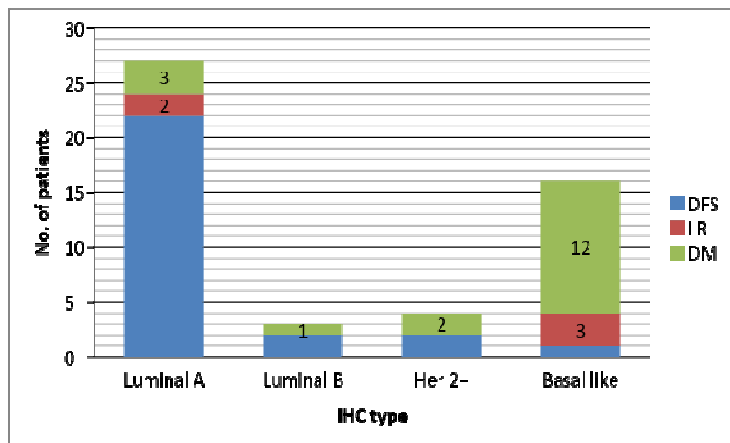
Graph 3: IHC Related Prognosis In Postmenopausal Breast Cancer Patients
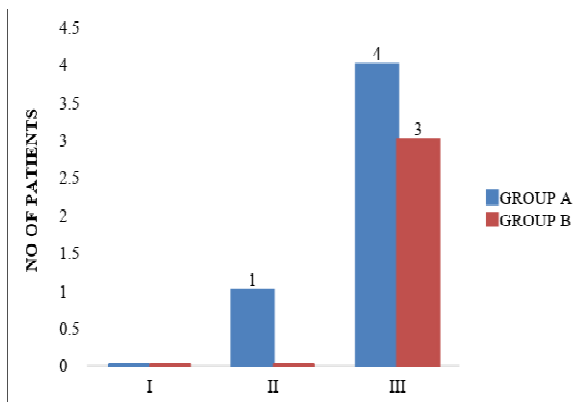
Graph 4: Staging Related Local Recurrence In Pre And Postmenopausal Breast Cancer Patients

Discussion:

Previously breast cancer was consider the disease of old age and its incidence increases with age.[4,5] In this study majority of patients were between the third and fifth decade of their life, similar to studies reported from India and other Asian countries.[7,8,9,10] Mean age of presentation for breast cancer was a decade earlier compared with western patients in both groups. More than 50% of women included in the study were diagnosed before the age of 50 years, in contrast to the western settings where only 23% of women younger than 50 years presented with breast cancer.[11,12,13] In this study, majority of the patients in both groups were from a rural background, which was contradictory to the previous reports from India as well as United States, which show a higher incidence in urban population compared to the rural population.[10,14] The difference was possibly due to the fact that women in rural areas face substantial barriers in receiving preventive health care services and also our hospital caters to maximum patients from rural area, thus accounting for higher number of rural breast cancer patients. In both pre and

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postmenopausal breast cancer women incidence was more on the left side in the upper outer quadrant corroborating with the previous reports.[8] The possible explanation was that the left breast is bulkier and the upper outer quadrant has a relatively larger volume of breast tissue. As reported in most of the previous studies, infiltrating duct cell carcinoma was the prominent histopathological type in both group.[7,8,9] Other types include lobular, medullary and fibroadenoma. In this study, luminal A subtype was the most prevalent in both groups. However, basal cell-like subtype was more prevalent in premenopausal breast cancer, similar to previous International and national studies.[15,16,17] Majority of the patients were diagnosed at stage III collaborating with the epidemiological data.[11] This reflects that the population lacked awareness of the disease. In this study, it was found higher stage was associated with premenopausal breast cancer corroborating with the previous reports.[18]

Treatment of breast cancer should be multidimentional and multidisciplinary in nature and must be given based on the stage of the disease, but it was found in the study majority of the patients irrespective of their stage of disease received adjuvant treatment in which surgery was complemented by either chemotherapy or radiotherapy or both. Usually combination of both chemotherapy and radiotherapy was given after surgery. . In this study adjuvant chemotherapy was given to all patients in both groups. As for the type of chemotherapy, more anthracycline plus taxanes regimens were given to premenopausal breast cancer patients, due to larger tumor sizes, more positive lymph nodes, more negative hormone receptors, higher tumor grades in this group, also reported in previous study.[17] Adjuvant hormonal therapy was given to all patients with positive hormone receptor. Chemotherapy induced neutropenia and G.I. symptoms were more associated with postmenopausal breast patients corroborating with the previous reports.[19]

Due to high workload and machine utilization, hypofractionation RT was prefered in our centre ranged from 40 - 45 gy in 13 - 17 fractions over 3 weeks period. radiation induced dermatitis was reported in (62%,70%) and found independent of menopausal status.

The relation between tumor size and lymph node involvement is well known and it is the only most powerful indicator of poor prognosis in breast cancer.[20] In this study also stage III showed worst prognosis with 38% and 30% Distant metastasis in pre and postmenopausal breast cancer, which indicates premenopausal breast cancer patients had a tendency to have higher stage and poorer prognosis, similar results also reported in other studies.[17] In this study, a very strong association was also detected between ER, PR, and Her 2 Neu expression with menopausal status and local, distant metastases. In both groups Luminal A subtype showed best prognosis with only one patient reported distant metastasis in postmenopausal breast cancer. ER, PR negativity and Her 2 Neu positivity was found to be associated with worsening disease with presence of distant metastases, similar results have been reported in other studies[21]. This was due to lack of awareness and poverty to afford anti-her2 monoclonal antibody(Transtuzumab). Basal cell-like subtype was more prevalent in premenopausal breast cancer and had worst prognosis with 18% LR and 66%DM in this group, corroborating with the previous global reports[22,23]. Overall prognosis in premenopausal breast cancer patients were poorer than postmenopausal breast cancer patients, corroborating with the previous reports.[17,24,25]

Conclusion:

In this comparative study, it was found that mean age of presentation for breast cancer was a decade earlier compared with western patients in both pre and postmenopausal breast cancer patients. Majority of the patients were diagnosed at stage III, it was found problem of late presentation was mainly due to rural background, poverty and lack of awareness. This study shows premenopausal breast cancer had a tendency to have larger tumor sizes, more positive lymph nodes, more negative hormone receptors and there was a relation between all of these features and more aggressive tumors and poorer prognosis.

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