

Comparison of Histopathological Features of Breast Cancer in Young and Elder Women

AMIKA KOUR¹, IKRAM ULLAH KHAN², MOHAMMAD SHARIF SHARIF³, MATIULLAH HAMDARD⁴, HUMA ZIA⁵, PORDIL KHAN⁶

¹Surgical D Ward, Khyber Teaching Hospital, Peshawar.

²Combined Military Hospital, Abbottabad.

³Head of Pathology department at Jamhoriat Hospital, National Cancer Control Program.

⁴Mphil Histopathology, Institute of Basic Medical Sciences, Khyber Medical University, Peshawar.

⁵Assistant Professor, Doctor of Physical Therapy, Allied Health Sciences, Iqra National University, Peshawar.

⁶Assistant Professor, Pathology Department, Khyber Medical College, Peshawar.

Corresponding author: Pordil Khan, Email: pordilk@yahoo.com

ABSTRACT

Background: One of the major causes of mortality in females worldwide is breast cancer. It is evident from previous studies that breast cancer is significantly different clinicopathologically in young women than in older women. In contrast, other studies have found no such evidence.

Objective: The current study's purpose was to compare breast cancer prevalence among young women to that in older patients regarding clinicopathological features and prognostic factors.

Material and Methods: All the included patients with lesions in the breast were diagnosed via sonography/mammography and later subjected to histopathological biopsy. Who had undergone mastectomy or surgery for breast conservation, Adjuvant chemotherapy, tamoxifen, and radiation therapy as possible treatment choices. Tumour size, lymph node condition, histological grade, mitotic rate, oestrogen p53, the MIB-1 proliferation index, the prevalence of levels of estrogen receptors, c-erbB2 expression, and these components were analyzed using immunohistochemistry and histopathology. Prognostic comparisons were performed to those for women with this disease 60 years of age and older with a focus on it occurring or appearing again,

Results: Clinical and pathological evaluations were performed on 40 patients with operable breast cancer under 40 and 80 patients older than 60 years. Elderly patients with breast cancer had a more aggressive phenotype than younger ones, with larger tumours (with 25 (31.25%) patients diagnosed with tumour size more than 5 cm), more lymph nodes involved, and greater levels of c-erbB2 (42 (52.5%) patients). However, these were typically only present in more advanced stages. Despite higher positive ER (34 (42.5%) patients) and PR (34 (42.5%) patients), additionally, a greater MIB-1 proliferation index (54 (67.5%) individuals) was observed in the elderly group compared to younger patients. Even though tamoxifen treatment and adjuvant chemotherapy became more popular. The rates of setback or re-appearing of the tumour, metastasis (30 (37.5%) individuals), and mortality (30 (37.50%) participants) were still more remarkable in elder patients.

Conclusion: It is concluded that in Pakistan, the prognosis associated with breast cancer in young adults is poor.

Keywords: p53, MIB Breast cancer, women – 40, fibroadenoma, papilloma

INTRODUCTION

Globally, breast cancer is the most common malignancy in women, and it is the second leading cause of cancer-related deaths (1). In the United States, only 5% to 7% of breast cancer cases are diagnosed in people under 40 (2-4); however, this number is much higher in developing countries in Asia and Africa (5-7). Compared to patients in higher-income nations, breast cancer patients in low- to middle-income (LMIC) countries frequently have advanced illnesses. Age and stage at presentation differ between high-income and low-income countries for racial and ethnic differences, varying environmental exposures, access to screening and treatment, and population distribution in developing nations like Pakistan, Afghanistan, India, and Bangladesh. We do not yet understand the aetiology of these discrepancies. The LMICs also have a large proportion of younger people, a short average life expectancy, and a high birth rate. (5-7). So, patients in these countries where women are diagnosed with breast cancers are in an advanced stage with increased aggression, as reported in multiple studies from developed and developing countries (8-10). So, it is of notice that up to date, a few studies were reported from Pakistan according to our knowledge. Women in Pakistan are more prone to breast malignancies, considered the most common among women in Pakistan. Approximately among all the malignancies in Pakistani women, breast cancer accounts for 40% (11, 12). Moreover, a detailed study of breast cancers among young females, its distribution and the clinicopathologic features compared to the older ones are not well studied. We sought to determine the incidence of breast cancer in the younger population and its comparison with aged patients.

MATERIALS AND METHODS

Individuals with breast cancer that can be operated on under 40 were evaluated clinically and pathologically. Initially, all the

participants were screened for any lesion in the breast. For women aged less than 40 years, sonography was performed whilst mammography was posing to be the screening method for older participants. Upon any lesion detected radiologically, the biopsy samples were sent to the histology section for further processing. The following factors were assessed: oestrogen and progesterone receptors, lymph node metastasis, histological grade, mitotic index, tumour size, expression of c-erbB2, p53, and the MIB-1 proliferation index. The Department of Histopathology, Pathology, Combined Military Hospital Peshawar, Pakistan, examined histopathology via hematoxylin-eosin (HE), immunohistochemistry utilizing the method of the avidin-biotin-peroxidase complex, as well as paraffin-embedded sections for antigen retrieval. Radiation therapy, breast-conserving surgery, or a modified radical mastectomy were used as treatments. Tamoxifen hormonal treatment and adjuvant chemotherapy with cyclophosphamide, methotrexate, and 5-fluorouracil (CMF) or adriamycin and cyclophosphamide (AC) were administered as needed. Prospectively, the patients were monitored until death, recurrence, or distant metastases. Clinicopathological factors were compared to those for breast cancers that could be operated on in patients 60 years and older.

RESULTS

Tables 1 and 2 show the Breast Cancer Cases characterized as operable in which patients younger than 40 years and above 60 years of age were included. In this study, 120 samples of Breast Cancer Cases were clinically investigated in which 40 (33.3%) patients were recorded whose age is less than 40 years, and 80 (77.7%) patients have recorded whose age is above 60 years. According to clinical investigation, 28 (70%) out of 40 patients received Adjuvant chemotherapy under 40 years old and 41 (51%) out of 80 above 60 years old. A total of 33 (82.5%) of patients received Adjuvant tamoxifen under 40 years and 65 (81.25%)

above 60 years of age, which is higher than the elderly age group. Relapse or re-occurrence and metastasis were higher in the older people in this study in comparison to younger patients, 39 (48.75%) and 30 (37.5%), to 10 (25%) and 6 (15 %), respectively. A total of 7 (17.5%) of patients recorded that they had a lower Mitotic index, whilst 13 (32.5%) of patients recorded that they had an intermediate Mitotic index and 20 (50%) of patients recorded that they had a High Mitotic index for under 40 years, while the mitotic index for the women above than 60 years was 30 (37.5%) Figure 1. The mitotic index for the younger age group was recorded as higher than the elder group age.

Table 1: Indicates the characteristics of cases of operable breast cancer in patients older than 60 years.

Variable	Category	Number	Percentage
Tumour size	0-2	13	16.25%
	>2-5	42	52.5%
	>5cm	25	31.25%
Grade	Low	12	15%
	Intermediate	56	70%
	High	12	15%
ER	Positive	40	50%
	Negative	40	50%
PR	Positive	34	42.5%
	Negative	46	57.5%
MIB-1proliferation Index	Positive	54	67.5%
	Negative	26	32.5%
C-erB	Positive	42	52.5%
	Negative	38	47.5%
Mitotic Index	Low	14	17.5%
	Intermediate	31	38.75%
	High	35	43.75%
Adjuvant Chemotherapy	Yes	41	51.25%
	No	39	48.75%
Adjuvant Tamoxifen	Yes	65	81.25%
	No	15	18.75%
Death	Death	30	37.5%
	Alive	36	45%
	Unknown	14	17.5%
Recurrence	Yes	39	48.75%
	No	41	51.25%
Metastasis	Yes	30	37.5%
	No	50	62.5%
Opinion	Fibroadenoma	17	21.25%
	Squamous Cell papilloma	23	28.75%
	Fibrocytic Disease	19	23.75%
	Infiltrating Ductal Carcinoma	21	26.25%

Table 2: Depicts the characteristics of breast cancer cases that can be operated on in patients under 40 years.

Variable	Category	Number	Valid Percentage
Tumour size	0-2	13	32.5%
	>2-5	21	52.5%
	>5cm	6	15%
Grade	Low	11	27.5%
	Intermediate	21	52.5%
	High	8	20%
ER	Positive	17	42.5%
	Negative	23	57.5%
PR	Positive	13	32.5%
	Negative	27	67.5%
MIB-1 proliferation Index	Positive	14	35%
	Negative	26	65%
C-erB	Positive	11	27.5%
	Negative	29	72.5%
Mitotic Index	Low	7	17.5%
	Intermediate	13	32.5%
	High	20	50%
Adjuvant Chemotherapy	Yes	28	70%
	No	12	30%
Adjuvant Tamoxifen	Yes	33	82.5%
	No	7	17.5%
Death	Death	15	37.5%
	Alive	18	45%
	Unknown	7	17.5%
	Yes	10	25%

Recurrence	No	30	75%
	Yes	6	15%
Metastasis	No	34	85%
	Yes	6	15%
Opinion	Fibroadenoma	9	22.5%
	Squamous Cell papilloma	12	30%
	Fibrocytic Disease	11	27.5%
	Infiltrating Ductal Carcinoma grade II	8	20%

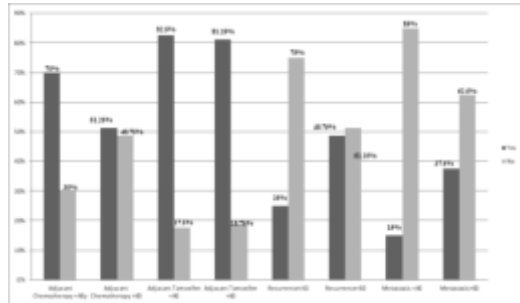


Figure 1: Shows the multiple bar chart of key features of Breast Cancer (operable) Cases in Patients Aged <40years and >60 years.

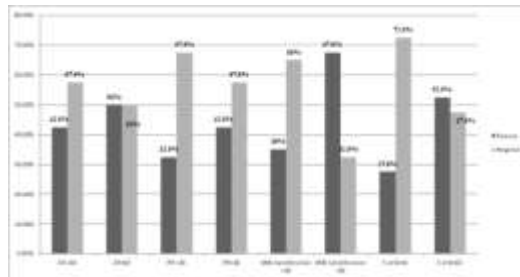


Table 2: Shows the positivity of histological markers in breast specimen

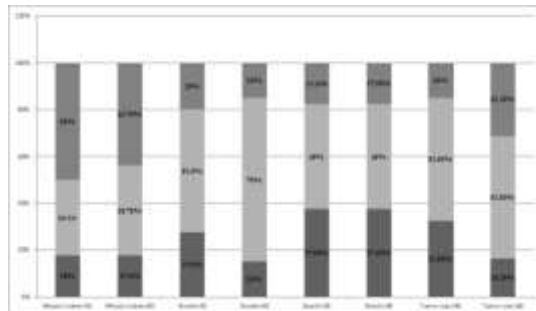


Figure 3: Shows the grade of cancer, tumour size and death ratio.

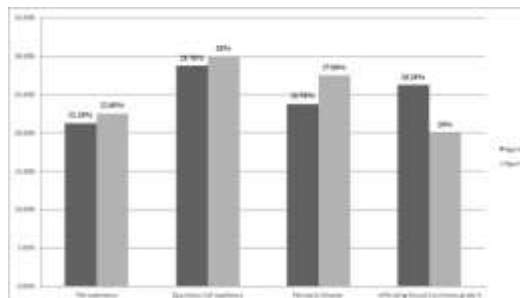


Figure 4: Shows the distribution of different types of carcinomas in the age group less than 40 years and above 60 years

DISCUSSION

In this study, 120 breast cancer patients of breast cancer were studied. However, due to shortcomings associated with the

facilities, they were not analyzed and studied clinically, histopathologically, or immunohistochemically. The majority of breast cancer cases in women under the age of 40 had stage IIA disease, positive lymph node tumours with a diameter of bigger than two cm, high grade, MIB-1 proliferation and a high mitotic index. It was found that women aged 60 years or above were less prone to breast cancer or less prevalent than at young age. The same was reported in one of the studies by Sundquist et al. (2002). Their study showed that compared to patients who were elderly, young patients had tumours that were larger and included more lymph nodes. Most of the patients in the latter group had clinical stage IIIB breast cancer, tumours bigger than two in centimetres, and tested positive for p53, MIB-1, c-erbB2, ER, PR, and were younger than 40 years old. However, the histological grade and mitotic rate of the young group were less than those of the elderly group. Sundquist's study contradicted itself by showing that the prevalence of stage 3 tumours rose irrespective of whether the individual is young or old and showed that it could rise with an increase in age (13, 14). It is reported that tumours had significant proliferation rates when they were young. Most of them had positive ER and PR tests, however, less frequently than in the group of elderly people. The reports were not analogous to several academic papers, as reported by Sidoni. et al., 2003; Daidone et al., 2003 that patients with older age having breast cancer typically had elevated ER and PR positive in contrast to patients with young age (15, 16). Theoretically, despite the fact that elevated ER and PR levels are thought to be a risk factor for breast cancer, this group of young individuals still responds to hormonal therapy or modification 2001 (17).

The majority of young patients (27.5%) displayed positive c-erbB2 expression, which was less than the elderly (52.5%) group. It appears that the latter group of patients exhibited more aggressive behaviour. Rodrigues et al. (2003) also found that younger people seemed to have higher percentages of c-erbB2 overexpression (18, 19). Sidoni et al. (2003) reported that younger breast cancer patients had more c-erbB2 expression than older patients, but this c-erbB2 expression in young patients was nearly comparable to Agrup's study. Results showed that the proportion of young patients with high levels of c-erbB2 protein expression was just 27% (15). To determine c-erbB2 amplification at the DNA level, evaluation using FISH (Fluorescent In Situ Hybridization) or MLPA (Multiplex Ligation-dependent Probe Amplification) is necessary (20, 21). Low p53 positive in the older group suggested that somatic mutation, rather than genetic mutation, may be more important in cancer development in this patient population. High p53 positivity indicated that tumours at young ages might have high genetic instability.

Compared to the older group, most young patients had had adjuvant chemotherapy and tamoxifen. Giving adjuvant chemotherapy appears to be the proper choice because young patients are considered a high-risk population. Even though adjuvant chemotherapy was administered more frequently to younger patients than to elderly individuals, the younger group experienced fewer death, recurrence, and metastasis. This disease appears to be caused by a high proliferation rate, which makes tumours in young people less aggressive. Older women survived more as compared to patient populations with young, but overall survival of women with breast cancer under 50 has considerably improved in the past decades. This is consistent with the study by Grosclaude et al. (2001), which found that the mortality in women under 40 years was slightly higher than 40 to 54 years old (22). Although elderly patients typically had more advanced breast cancer, whilst young women showed a more aggressive phenotype. Despite receiving chemotherapy, radiotherapy, and tamoxifen, younger individuals still had greater relapse rates, metastasis, and mortality. The molecular study is required, especially for patients of Asian ethnicities, as it appears that the biological behaviour of breast cancer in young and older women differs from countering the menace of breast cancer among the female population.

CONCLUSION

It is concluded in this study that the elderly population of Pakistan are more prone to breast cancer, followed by the younger ones. Comparatively, the death ratio is higher in the elderly population than in women younger than 40 years. Moreover, routine examinations for different types of carcinomas, especially breast cancers according to standard guidelines, are needed. Furthermore, awareness at the national and international levels regarding breast cancer is necessary.

REFERENCES

1. Paluch-Shimon S, Peccatori FJAoO. BRCA 1 and 2 mutation status: the elephant in the room during oncofertility counseling for young breast cancer patients. 2018;29(1):26-8.
2. Anders CK, Johnson R, Litton J, Phillips M, Bleyer A, editors. Breast cancer before age 40 years. *Seminars in oncology*; 2009: Elsevier.
3. Brinton LA, Sherman ME, Carreon JD, Anderson WFJJotNCI. Recent trends in breast cancer among younger women in the United States. 2008;100(22):1643-8.
4. Assi HA, Khoury KE, Dbouk H, Khalil LE, Mouhieddine TH, El Saghir NSJJotd. Epidemiology and prognosis of breast cancer in young women. 2013;5(Suppl 1):S2.
5. Akarolo-Anthony SN, Ogundiran TO, Adebamowo CAJBcr. Emerging breast cancer epidemic: evidence from Africa. 2010;12(4):1-4.
6. Jazayeri SB, Saadat S, Ramezani R, Kaviani AJCe. Incidence of primary breast cancer in Iran: Ten-year national cancer registry data report. 2015;39(4):519-27.
7. El Saghir NS, Khalil MK, Eid T, El Kinge AR, Charafeddine M, Geara F, et al. Trends in epidemiology and management of breast cancer in developing Arab countries: a literature and registry analysis. 2007;5(4):225-33.
8. Fredholm H, Magnusson K, Lindström LS, Garmo H, Fält SE, Lindman H, et al. Long-term outcome in young women with breast cancer: a population-based study. 2016;160(1):131-43.
9. Brandt J, Garne JP, Tengrup I, Manjer JJJWjoso. Age at diagnosis in relation to survival following breast cancer: a cohort study. 2015;13(1):1-11.
10. Chen H-I, Zhou M-q, Tian W, Meng K-x, He H-fJPo. Effect of age on breast cancer patient prognoses: a population-based study using the SEER 18 database. 2016;11(10):e0165409.
11. Khaliq SA, Naqvi SB, Fatima AJS. Retrospective study of cancer types in different ethnic groups and genders at Karachi. 2013;2(1):1-6.
12. Sarwar MR, Saqib AJCM. Cancer prevalence, incidence and mortality rates in Pakistan in 2012. 2017;4(1):1288773.
13. Sundquist M, Thorstenson S, Brudin L, Wingren S, Nordenskjöld BJTb. Incidence and prognosis in early onset breast cancer. 2002;11(1):30-5.
14. Sundquist M, Thorstenson S, Brudin L, Wingren S, Nordenskjöld BJEJoC. Incidence and prognosis in early-onset breast cancer. 2001(37):41-2.
15. Sidoni A, Cavaliere A, Bellezza G, Scheibel M, Bucciarelli EJTB. Breast cancer in young women: clinicopathological features and biological specificity. 2003;12(4):247-50.
16. Daidone MG, Coradini D, Martelli G, Veneroni SJCrtoh. Primary breast cancer in elderly women: biological profile and relation with clinical outcome. 2003;45(3):313-25.
17. Clemons M, Goss PJNEJoM. Estrogen and the risk of breast cancer. 2001;344(4):276-85.
18. Rodrigues NA, Dillon D, Carter D, Parisot N, Haffty BGJCIJotACS. Differences in the pathologic and molecular features of intraductal breast carcinoma between younger and older women. 2003;97(6):1393-403.
19. Rosser RJCIJotACS. Differences in the pathologic and molecular features of intraductal breast carcinoma between younger and older women. 2003;98(5):1102-3.
20. Schouten JP, McElgunn CJ, Waaijer R, Zwijnenburg D, Diepvens F, Pals GJNar. Relative quantification of 40 nucleic acid sequences by multiplex ligation-dependent probe amplification. 2002;30(12):e57-e.
21. Schmidt M, Lewark B, Kohlschmidt N, Glawatz C, Steiner E, Tanner B, et al. Long-term prognostic significance of HER-2/neu in untreated node-negative breast cancer depends on the method of testing. 2005;7(2):1-11.
22. Brenner H, Hakulinen TJJoCO. Are patients diagnosed with breast cancer before age 50 years ever cured? 2004;22(3):432-8.