INVESTIGATING RADIOLOGICAL INSIGHTS OF BREAST CANCER WITH AGE AT JINNAH POSTGRADUATE MEDICAL CENTRE, KARACHI

SALDERA KA*[1], KHAN TA[2], SAMO UBK[3], MEHBOOB S[4]

[1]*Department of Physiology, Basic Medical Sciences Institute, JPMC Karachi, Pakistan*
[2]*Department of Physiology, University of Karachi, Pakistan*
[3]*Department of Physiology, Basic Medical Sciences Institute Karachi, Pakistan*
[4]*Department of Pharmacology, Jinnah Post Graduate Medical Centre, Karachi, Pakistan*
*Corresponding author's email address: k.salderabbas@gmail.com

Abstract: *There is a conflicting opinion regarding the association between age and breast cancer in women. This study was conducted to investigate the histopathological findings of findings and features of diagnosed patients of breast cancer about their age and radiological findings of lesions and to determine the relation of aggressive findings in different age groups.* **Methods:** *A cross-sectional study was conducted in the Radiological Department, JPMC, Karachi, from September 2022- September 2023. To ascertain if the histological characteristics of the tumors were connected to the age of the patient, the histology reports of 100 women with breast cancer diagnoses underwent examination. Grading of their cancer based on BIRAD Classification was done on the radiological findings of ultrasound and mammography. Patients between 15 and 65 years were split into five different age groups. Patients who were naive and had never had any surgical or medicinal treatment for cancer before were included. After obtaining consent, a detailed questionnaire with the required data and physical and chemical parameters was completed. Tissue samples in studies mainly included trust biopsies, large mass removal, and tissues from mastectomies.* **Results:** *People under the age of 40 were shown to have a higher incidence of grade III infiltrating ductal carcinoma (P 0.0001). Lobular carcinomas were observed more frequently in the elderly group. With advancing age, there was a discernible decline in lymphoplasmacytic stromal response, axillary lymph node metastases, and vascular invasion, all unaffected by tumor grade.* **Conclusion:** *These findings imply that the histology of breast cancer may alter with age and that older patients may exhibit less aggressive characteristics in some circumstances.*

Keywords: Age Groups, Breast Cancer, Cancer, Radiology

Introduction

Breast cancer is a widely recognized complicated disease due to the high combination of hereditary and non-genetic risk factors associated with this disease. The worldwide prevalence of Breast cancer is high in both developed and less developed worlds (1). Breast cancer is ranked 2nd in most frequently diagnosed cancer in females and the most common cause of death in females. According to a recent World Health Organization [WHO] survey, more than 1.2 million people receive a breast cancer diagnosis each year in the world. It is estimated that worldwide, over 632,000 women died from breast cancer (2). Pakistan is ranked high as compared to other Asian countries in the frequency of breast cancer. Women are generally diagnosed at an early age and with advanced disease. It ranks as the second leading cause of death for American women (3). Approximately 15% to 20% of all breast cancer cases are familial. Inherited mutations in essential genes linked to breast cancer account for 5–10% of all cases of the disease (4). According to estimates from the International Agency for Research on Cancer (IARC), there were 8.2 million cancer-related deaths and 14.1 million new diagnoses worldwide in 2012 (5). Few studies suggested that cancer of any type, especially breast cancer, doesn't have any influence or adverse effects of age on its progression. At the same time, some studies confirmed the link between increasing age and the progression of cancer. Comparatively, very few studies on histopathological features of breast cancer are done in Pakistan, which could help better understand its relation with age on histology. However, another study indicates that young women with breast cancer have a relatively worse prognosis but a fair prognosis in the elderly. According to other studies, the disease's behavior is unaffected by age (6,7). Recent years have seen a shortage of investigations comparing the histological characteristics of both young and elderly of breast cancer. The purpose of this study is to investigate the histopathological findings and features of diagnosed patients of breast cancer about their age and radiological findings of lesions and to determine the relation of aggressive findings in different age groups.

Methodology

A cross-sectional study was conducted on 100 women who were diagnosed with breast cancer; grading of their cancer based on BIRAD Classification was done on the radiological findings of ultrasound and mammography at the Radiological Department, Jinnah Postgraduate Medical Center, Karachi. The patients were divided into five age groups: 15-24 years, 26-35 years, 36-45 years, 46-55 years, and 56-65 years. Ages 15 to 45 were considered to be premenopausal, while 46 to 65 were considered to be post-menopausal. The age groups of 15-45 years and 45-65 years

were compared because some premenopausal and perimenopausal patients fall into the 50-60 age range. A questionnaire with an anthropometric profile, reproductive history, and history related to Breast cancer, family history, use of Contraceptives, diet, drug history, and lifestyle was filled out after taking consent along with physical and chemical parameters. Tissue samples were collected for histopathological assessment.

Tissue samples included in studies were mainly trust biopsies, some wedges and cone biopsies, large mass removal, excision biopsies, and tissues from mastectomies. The histological type, tumor grade, lymphatic and blood vessel invasion, tumor necrosis, and degree of stromal lymphoplasmacytic response were all investigated in pathology studies.

The five age groups were compared statistically using the chi-squared test. Multivariate logistical regression was performed using STATA software to produce independent age group predictions. If P 0.05, a finding was deemed statistically significant.

Results

There were 100 women in the study aged from 15 to 65 years. Five groups were formed: Group A: 15-24 years, Group B: 26-35 years, Group C: 36-45 years, Group D: 46-

55 years, and Group E: 56-65 years. There were significant differences concerning disease advancement Table 1.

Table 1: Distribution of study participants concerning age

Age (Years)	N (%)
15 – 25	2 (2%)
26 – 35	25 (25%)
36 – 45	33 (33%)
46 – 55	24 (24%)
56 – 65	16 (16%)
Mean ± Std. Deviation	42.61±10.81

Group A presented with complaints like pain, cystic feeling, and swelling increase in size; on BIRAD Scores, almost the entire group Fell in categories 2, 3, and 4, varying with persons; some had just one side involvement, and some had both sides involved. Group B shows some invasive. This age group has a central High-grade malignant tumor and spindle cell lesion consistent with malignant, mostly with the BIRAD 4 category. In Group C, D, and Group E, women were reported to have many vulnerable tumors, ranging from Invasive Ductal Carcinoma Grade I and III to infiltrating tumors grade III, and large mucinous tumors were reported (Table 2).

Table 2: Disease presentation in study groups

Age	Group A	Group B	Group C	Group D	Group E
	15-24 years	**26-35 years**	**36-45 years**	**46-55 years**	**56-65 years**
Complaint	• Pain, • Cyst appearance, • Swelling increase in size	• Pain, • Cyst appearance, Swelling increase in size	• Pain, • Cyst appearance, • Swelling increase in size	• Pain, • Cyst appearance, • Swelling increase in size	• Pain, • Cyst appearance, • Swelling increase in size
Birad Category	0, 1, 2	2, 3	2,3	3,4	5,6
Pathology	• Fibro-adenomas • Cyst • Sebaceous cyst	• Fibro-adenomas • Cyst • Sebaceous cyst • Phyllodes • Features of Ductectecia • Lymph-adenopathy	• Fibro-adenomas • High-grade tumors • Invasive ca grade I, II	• More vulnerable tumors • High-grade tumors with metastasis • Invasive ca grade III	• Late-stage tumors with metastasis • Invasive ca grade III, IV
Metastasis	NONE	NONE	localized	Distant metastasis	Distant metastasis and organ involvement

Discussion

Different opinions are given in aspect to how age is related to the prognosis and progression of breast cancer. Many clinicians had the impression that young females are more likely to have the aggressive disease than older females, where carcinoma is idle (8, 9). This study was carried out to evaluate this idea further. The results of this study show that aggressive tumors can occur in any age group. Although the increased incidence of aggressive tumors is higher in middle-aged women, with complaints of pain, hard lump,

swelling increase in size, presence of a cyst, needle-like pricking pain, and sometimes fever with duration lasting from 1 week to 7 months in different women and mostly category 2, 3 and 4 are found in this category, while in older women just pain, swelling size increase and sometimes no sign and symptoms at all with no long duration of illness presented invasive carcinomas. However, more incidences of the aggressive nature of tumors do not suggest a less favorable prognosis in young women, but early detection does have an impact on its prognosis. These results do not comply with other studies, which suggest a diagnosis of

more aggressive cancers in older women, often incurable metastatic tumors, while younger women are at a higher risk of developing triple-negative or HER-2 positive cancers (10, 11). Literature reports that tumors with low BIRAD scores also tend to metastasize rapidly in older women, making them incurable and inaccessible. A study conducted on 564 women with breast cancer studied the spread of cancer to a distant site with increasing age (12). The results revealed a high incidence of brain metastasis in younger women and lung metastasis in older women, which indicates a difference in tropism of distant metastasis depending upon the type of breast cancer.

It is also noted that axillary lump nodes are involved in women with a high duration of illness. These results confirmed that early detection will get an early cure and fewer chances of metastasis (13, 14). Metastasis is seen in both extreme age groups. The involvement of lump nodes doesn't differ with age. The middle-aged group has a more defined margin of carcinoma than older women in the case of microscopic examination. As one of the studies suggested, with increasing age, the internal anatomy weakens, and this could be the reason behind this (15). Further studies should be done on whether our old bodies can sustain the cancer burden. The older population has particular tumor forms and metastatic patterns that are associated with a good prognosis (16, 17).

However, to achieve a maximum survival rate, every breast cancer type requires adequate treatment and management in any age group. Furthermore, the 5-year survival rate is comparable to that of women under the age of 60, and there is no increase in morbidity when treating any senior women who are 60 years of age or beyond (18). Medullary carcinoma patients have been found to have much lower mean ages than lobular and mucoid carcinoma patients, who tend to be older patients on average. In older women, intracystic papillary cancer is also more common (19). Additionally, it has been hypothesized that young women develop higher-grade tumors that are more aggressive than older women. However, contradictory to this, another study found a higher prevalence of lobular cancers in younger women (20).

The vast majority of screening mammograms fall into BI-RADS 1 and 2. Screening mammograms with suspicious findings should generally be assigned BI-RADS 0 to indicate a call back for diagnostic evaluation, meaning additional views to confirm and further evaluate the finding. The results do not suggest that older breast cancer patients require more aggressive treatment than younger individuals. When making therapy options, consider the patient's general well-being, physical condition, and emotional state. Consider the histological characteristics of the disease rather than just the patient's age.

Our study has limitations. The study sample is very small, and women were selected from the same hospital with little to no variability in demographics. A large multi-centered study will yield better results.

Conclusion

These findings imply that the histology of breast cancer may alter with age and that older patients may exhibit less aggressive characteristics in some circumstances. The study analysis showed that various instances fit into the five BIRAD categories. It can also be tentatively said that hormones play a crucial role in the progression and prognosis of tumors.

Declarations

Data Availability statement
All data generated or analyzed during the study are included in the manuscript.
Ethics approval and consent to participate.
Approved by the department concerned. (IRB/JPMC-8-21/R091)
Consent for publication.
Approved
Funding
Not applicable

Conflict of interest

The authors declared the absence of a conflict of interest.

Author Contribution

KAUSAR ABBAS SALDERA (Associate Professor)
Coordination of collaborative efforts.
Study Design, Review of Literature.
Conception of Study, Development of Research Methodology Design, Study Design, manuscript Review, and final approval of manuscript.
TASEER AHMED KHAN (Professor)
Conception of Study, Final approval of manuscript.
Manuscript revisions, critical input.
UFAQUE BATOOL K. SAMO (M.Phil. Student)
Coordination of collaborative efforts.
Data acquisition, analysis
SYED MEHBOOB (Professor)
Manuscript drafting.
Data entry and data analysis, as well as drafting the article.

References

1. Lukasiewicz S, Czeczelewski M, Forma A, Baj J, Sitarz R, Stanisławek A. Breast cancer—epidemiology, risk factors, classification, prognostic markers, and current treatment strategies—an updated review. Cancers. 2021 Aug 25;13(17):4287. https://doi.org/10.3390/cancers13174287

2. Kumar A, Singla A. Epidemiology of breast cancer: current figures and trends. Preventive oncology for the gynecologist. 2019:335-9. https://doi.org/10.1007/978-981-13-3438-2_26

3. Ali A, Manzoor MF, Ahmad N, Aadil RM, Qin H, Siddique R, et al. The burden of cancer, government strategic policies, and challenges in Pakistan: A comprehensive review. Front Nutr. 2022 Jul 22; 9:940514. https://doi.org/10.3389/fnut.2022.940514

4. Exman P, Tolaney SM. HER2-positive metastatic breast cancer: A comprehensive review. CAH&O. 2021 Jan 1;19(1):40-50.

5. Todua F, Gagua R, Maglakelidze M, Maglakelidze D. Cancer incidence and mortality-Major patterns in GLOBOCAN 2012, worldwide and Georgia. Bull. Georgian Natl. Acad. Sci. 2015;9(1):168-73.

6. Chen HL, Zhou MQ, Tian W, Meng KX, He HF. Effect of age on breast cancer patient prognoses: a population-based study using the SEER 18 database. PloS one. 2016 Oct 31;11(10):e0165409. https://doi.org/10.1371/journal.pone.0165409

7. Zaheer S, Shah N, Maqbool SA, Soomro NM. Estimates of past and future time trends in age-specific breast cancer incidence among women in Karachi, Pakistan: 2004–2025. BMC public health. 2019 Dec;19:1-9. https://doi.org/10.1186/s12889-019-7330-z

8. Moon HJ, Kim EK, Kim MJ, Yoon JH, Park VY. Comparison of clinical and pathologic characteristics of ductal carcinoma in situ detected on mammography versus ultrasound only in asymptomatic patients. Ultrasound Med Bio. 2019 Jan 1;45(1):68-77. https://doi.org/10.1016/j.ultrasmedbio.2018.09.003

9. Johnson RH, Anders CK, Litton JK, Ruddy KJ, Bleyer A. Breast cancer in adolescents and young adults. PBC. 2018 Dec;65(12):e27397. https://doi.org/10.1002/pbc.27397

10. Bitencourt AG, Rossi Saccarelli C, Kuhl C, Morris EA. Breast cancer screening in average-risk women: towards personalized screening. Brit. J. Radiol.2019 Nov;92(1103):20190660. https://doi.org/10.1259/bjr.20190660

11. Monticciolo DL, Malak SF, Friedewald SM, Eby PR, Newell MS, Moy L, Destounis S, Leung JW, Hendrick RE, Smetherman D. Breast cancer screening recommendations inclusive of all women at average risk: update from the ACR and Society of Breast Imaging. JACR. 2021 Sep 1;18(9):1280-8. https://doi.org/10.1016/j.jacr.2021.04.021

12. Yazdani A, Yaseri M, Haghighat S, Kaviani A, Zeraati H. Investigation of prognostic factors of survival in breast cancer using a frailty model: a multicenter study. Breast Cancer: Basic Clin. Res. 2019 Sep; 13:1178223419879112. https://doi.org/10.1177/1178223419879112

13. Akrami M, Sepahdar A, Arasteh P, Tahmasebi S, Zangouri V, Askari A, Pezeshki B, Talei A. Do site and type of metastasis in breast cancer show a changing pattern with increased age? A cross comparison of clinicopathological characteristics between age groups. World J. Surg. Oncol. 2018 Dec;16(1):1-7. https://doi.org/10.1186/s12957-018-1435-1

14. Hu C, Hart SN, Gnanaolivu R, Huang H, Lee KY, Na J, et al. A population-based study of genes previously implicated in breast cancer. NEJM. 2021 Feb 4;384(5):440-51. DOI: 10.1056/NEJMoa2005936

15. Plichta JK, Thomas SM, Vernon R, Fayanju OM, Rosenberger LH, Hyslop T, Hwang ES, Greenup RA. Breast cancer tumor histopathology, stage at presentation, and treatment in the extremes of age. Breast Cancer Res Treat. 2020 Feb;180:227-35. https://doi.org/10.1007/s10549-020-05542-4

16. Beňačka R, Szabóová D, Guľašová Z, Hertelyová Z, Radoňák J. Classic and new markers in diagnostics and classification of breast cancer. Cancers. 2022 Nov 5;14(21):5444. https://doi.org/10.3390/cancers14215444

17. Schoemaker MJ, Nichols HB, Wright LB, Brook MN, Jones ME, O'Brien KM, Adami HO, Baglietto L, Bernstein L, Bertrand KA, Boutron-Ruault MC. Association of body mass index and age with subsequent breast cancer risk in premenopausal women. JAMA oncol. 2018 Nov 1;4(11):e181771-. doi:10.1001/jamaoncol.2018.1771

18. DeSantis CE, Miller KD, Dale W, Mohile SG, Cohen HJ, Leach CR, et al. Cancer statistics for adults aged 85 years and older, 2019. CA: Cancer J clin. 2019 Nov;69(6):452-67. https://doi.org/10.3322/caac.21577

19. Lyndin M, Hyriavenko N, Sikora V, Lyndina Y, Soroka Y, Romaniuk A. Invasive breast carcinoma of no special type with medullary pattern: morphological and immunohistochemical features. Turk J Pathol. 2022;38(3):205. doi: 10.5146/tjpath.2021.01559

20. Yazdani-Charati R, Hajian-Tilaki K, Sharbatdaran M. Comparison of pathologic characteristics of breast cancer in younger and older women. CJIM. 2019;10(1):42.doi: 10.22088/cjim.10.1.42