

ORIGINAL RESEARCH

Analysis of Clinico-radio-pathological Features and Biological Behavior of Breast Cancer in Young Indian Women: An Institutional Based Study

Shivendra Kumar Chaudhary¹, Pragya Sinha²

¹Associate Professor, ²Assistant Professor, Department of Radio diagnosis, Rama Medical College, Hospital & Research Center, Hapur, UP, India

Correspondence:

PragyaSinha

Assistant Professor, Department of Radio diagnosis, Rama Medical College, Hospital & Research Center, Hapur, UP, India

Email:pragya105@gmail.com

ABSTRACT

Background: Among women, incidence rates for breast cancer significantly exceeded those for other cancers in both transitioned and transitioning countries, it remaining as a remaining as most commonly diagnosed cancer and the prominent cause of cancer death in women worldwide. The present study was conducted to assess Clinico-radio-pathological Features and Biological Behavior of Breast Cancer in Young Indian Women.

Materials and Methods: A prospective descriptive study was done among women aged less than 40 years diagnosed with breast cancer. In patients with suspicious clinical or ultrasound findings or if biopsy yielded malignancy, digital mammography was performed. All the BI-RADS 4 and 5 lesions and few of the BI-RADS 3 lesions were biopsied, and samples were sent for histopathology (HPE) and immunohistochemistry (IHC) examinations. The data was collected on Microsoft Office Excel 2013 and statistical analysis was performed using IBM SPSS version 21(Illinois, Chicago). P value <0.05 was considered significant.

Results: A total of 300 patients who were less than 40 years of age were treated for breast cancer and the mean age was 35.8yrs. 15% patients gave a family history of breast cancer. Of 300 patients, 92.66% were symptomatic. Majority of the patients (52%) presented in III stage at the time of diagnosis. Infiltrating ductal carcinoma (IDC) with or without ductal carcinoma in situ (DCIS) was the most common histopathological diagnosis of breast cancer (91%), followed by pure DCIS in 2.33% and others (invasive lobular carcinoma, papillary carcinoma, medullary carcinoma, lymphoma and adenoid cystic carcinoma) in 6.66%. Of all the IDCs, 69.66% were moderate grade (grade II) and 27% were high grade (grade III). On IHC examinations, ER/PR were positive in 52% of breast tumours with Luminal A (ER/PR positive, Ki-67<14% and HER-2 negative) in 16% & Luminal B HER-2 negative (ER/ PR positive, Ki-67≥14% and HER-2 negative) in 44%, Luminal B HER-2 positive (ER/PR and HER-2 positive) in 9.33%, HER-2 enriched (HER-2 positive and ER/PR negative) in 6.3% and triple-negative breast cancer(ER/PR and HER-2 negative) in 47.33 % of patients. Digital mammography examinations were performed in 260 of 300 patients with breast cancer as an additional examination to the ultrasound if clinical or sonographic features were suspicious of malignancy or after the pathological diagnosis of malignancy. On digital mammography, breast cancers were suspected in 84.61% patients. Majority of the patients had either heterogeneously dense (ACR type C in

51.92%) or extremely dense (ACR type D in 42.30%) breast tissue. Mass without microcalcifications was detected in 50%, mass with microcalcifications in 38.63%, suspicious microcalcifications alone in 5.90% patients and architectural distortion in 5.45%. False-negative results were observed in 15.38% and all of them had dense breast tissue (ACR type C or type D). Breast ultrasound examinations were performed in all 300 patients and breast cancers were suspected in 93.33% and false negatives in 6.66% patients. On ultrasound, 90% patients demonstrated mass lesions, and 3.33% patients displayed non-mass lesion with or without ductal calcifications. Majority of the lesions were assigned either BI-RADS 4 (70%) or BI-RADS 5 (24.66%) category. The average tumour size on US was 3.5 cm.

Conclusion: The present study concluded that while ultrasound is the recommended imaging method for evaluation of breast under the age of 40 years, we found a better characterization of lesions and higher cancer detection rates when they were also evaluated with mammography.

Keywords: Ultrasound, Breast Cancer, Mammography.

INTRODUCTION

The breast is the glandular organ, which continuously changes physiologically throughout the reproductive age group and after that in women under the influence of hormones. Various breast structures give rise to different types of lesions, and clinical presentation varies from discomfort, pain, lump with pain/painless, skin changes and, anxiety.^{1,2} Breast cancer is the leading cause of cancer in India and accounts for 27.7% of all cancers in Indian women.³ Breast cancer is usually found in older women. However, there is an apparent higher incidence of breast cancer in younger Indian women compared to the West as nearly 75% of the Indian population is less than 50 years of age.⁴ The median age of presentation is almost a decade earlier than the western population. It is rare to find breast cancer in women less than 40 years of age in the West and it varies between 2 and 7% depending on the races and ethnicity.⁵ According to recent reports the breast cancer-related deaths are mainly due to the "incurable" nature of metastatic breast cancer (MBC). It is estimated that about 6% of patient have metastatic disease at the time of diagnosis and 20-50% patient first diagnosed with primary breast cancer will eventually develop metastatic disease. Even with the remarkable advances in research and clinical management, the current treatment strategies for breast cancer metastasis still largely rely on the use of systemic cytotoxic agents, which frequently deteriorate the patient's life quality due to severe side effects and, in many cases, have limited long-term success. Only 26% of patient are survive for 5-years, due to poor diagnosis for MBC patients. So, MBC remains the most challenging problem facing both cancer researcher and oncologist.⁶ The present study was conducted to assess Clinico-radiopathological Features and Biological Behavior of Breast Cancer in Young Indian Women.

MATERIALS AND METHODS

A prospective descriptive study was done among women aged less than 40 years diagnosed with breast cancer. Women were evaluated with breast ultrasound and/or digital mammogram or MRI, diagnosed with breast cancer on histopathology and molecular analysis by immunohistochemistry (IHC) examination for estrogen receptor (ER), progesterone receptor (PR), Ki-67 index and human epidermal growth factor (HER2-neu) expression done were included. Before the commencement of the study ethical approval was taken from the ethical committee of the institute and informed consent was taken from the patient. Women with a history of prior treatment of breast cancer with surgery, radiotherapy or chemotherapy were excluded from the study. On clinical evaluation, data included patient's age, indication for breast imaging, clinical manifestation (palpable mass, pain, nipple discharge or others),

family history (first or second-degree relatives) of breast cancer, personal history (underlying comorbidities, another malignancy or pregnancy) were collected. In patients with suspicious clinical or ultrasound findings or if biopsy yielded malignancy, digital mammography was performed. US examinations were performed on Siemens Acuson S2000 by 12-18 MHz high-resolution linear probe, mammography examinations on Senographe Essential digital mammography General Electric (GE) system and Imaging features were described using 5th edition ACR BI-RADS. All the BI-RADS 4 and 5 lesions and few of the BI-RADS 3 lesions were biopsied using 14-gauge BARD MAX-CORE disposable biopsy gun under US or mammography (used when only calcifications present, and the lesions were not visible on the US) guidance and samples were sent for histopathology (HPE) and immunohistochemistry (IHC) examinations. The histopathology slides were examined by experienced breast pathologists and reported according to WHO classification. Tumour grading was done according to the modified Bloom-Richardson grading system. ER, PR, Ki-67, and HER2-neu expressions were determined by IHC examination. In case of equivocal results of HER2-neu on IHC, Fluorescence in situ hybridization (FISH) test was done to confirm. The data was collected on Microsoft Office Excel 2013 and statistical analysis was performed using IBM SPSS version 21 (Illinois, Chicago). Student's unpaired t-test was used to calculate the difference in continuous variables, and Chi-square test or Fisher's exact test for categorical variables, with P value <0.05 was considered significant.

RESULTS

A total of 300 patients who were less than 40 years of age were treated for breast cancer and the mean age was 35.8 yrs. The patient's clinical and pathological characteristics were summarized in Table 1.

15% patients gave a family history of breast cancer. Of 300 patients, 92.66% were symptomatic. In 7.33% asymptomatic patients, breast cancers were detected on the mammography or MRI screening done because of positive family history or the patient's request before marriage or planning a pregnancy. Clinical suspicion of axillary lymphadenopathy was observed in 80% patients; however pathological diagnosis of metastatic lymph nodes was seen only in 70.33% patients. Majority of the patients (52%) presented in III stage at the time of diagnosis. Breast conservative surgery (BCS) was done more frequently (60%) than the mastectomy (40%). Infiltrating ductal carcinoma (IDC) with or without ductal carcinoma in situ (DCIS) was the most common histopathological diagnosis of breast cancer (91%), followed by pure DCIS in 2.33% and others (invasive lobular carcinoma, papillary carcinoma, medullary carcinoma, lymphoma and adenoid cystic carcinoma) in 6.66%. Of all the IDCs, 69.66% were moderate grade (grade II) and 27% were high grade (grade III). On IHC examinations, ER/PR were positive in 52% of breast tumours with Luminal A (ER/PR positive, Ki-67 <14% and HER-2 negative) in 16% & Luminal B HER-2 negative (ER/PR positive, Ki-67 ≥14% and HER-2 negative) in 44%, Luminal B HER-2 positive (ER/PR and HER-2 positive) in 9.33%, HER-2 enriched (HER-2 positive and ER/PR negative) in 6.3% and triple-negative breast cancer (ER/PR and HER-2 negative) in 47.33% of patients.

Imaging findings of digital mammography and ultrasound are summarised in Table 2.

Digital mammography examinations were performed in 260 of 300 patients with breast cancer as an additional examination to the ultrasound if clinical or sonographic features were suspicious of malignancy or after the pathological diagnosis of malignancy. On digital mammography, breast cancers were suspected in 84.61% patients. Majority of the patients had either heterogeneously dense (ACR type C in 51.92%) or extremely dense (ACR type D in 42.30%) breast tissue. Mass without microcalcifications was detected in 50%, mass with microcalcifications in 38.63%, suspicious microcalcifications alone in 5.90% patients and

architectural distortion in 5.45%. False-negative results were observed in 15.38% and all of them had dense breast tissue (ACR type C or type D).

Breast ultrasound examinations were performed in all 300 patients and breast cancers were suspected in 93.33% and false negatives in 6.66% patients. On ultrasound, 90% patients demonstrated mass lesions, and 3.33% patients displayed non-mass lesion with or without ductal calcifications. Majority of the lesions were assigned either BI-RADS 4 (70%) or BI-RADS 5 (24.66%) category. The average tumour size on US was 3.5 cm.

Table 1: Clinical, pathological and molecular characteristics of breast cancer in young women

Variables	N(%)
Age (years)	35.8
Family history (1st or 2nd degree)	
Positive	45(15%)
Negative	255(85%)
Symptomatic	278(92.66%)
Asymptomatic	22(7.33%)
Lymph nodes	
Clinical suspicion	240(80%)
Pathological	211(70.33%)
Clinical stage	
I	9(3%)
II	87(29%)
III	156(52%)
IV	48(16%)
Histopathology	
IDC±DCIS	273(91%)
DCIS	7(2.33%)
Others (mucinous, papillary, lobular carcinoma and metastasis)	20(6.66%)
Histologic grade	
1 (G1)	10(3.33%)
2 (G2)	209(69.66%)
3 (G3)	81(27%)
Biological markers and molecular subtypes	
ER/PR positive (LA+LB)	156(52%)
(a) ER/PR positive with Ki-67<14%	48(16%)
b) ER/PR positive with Ki-67>14% (LB HER-2 negative)	132(44%)
HER-2 expression	43(14.33%)
(a) ER/PR and HER-2 positive (LB HER-2 positive)	28(9.33%)
(b) ER/PR negative and HER-2 positive (HER-2 Enriched)	19(6.33%)
Triple negative	142(47.33%)

Table 2: Mammography and ultrasonography features of breast cancer in young women

Variable	N(%) N=260
Breast density	
ACR category A	0(0%)
ACR category B	15(5.76%)
ACR category C	135(51.92%)

ACR category D	110(42.30%)
Positive findings	220(84.61%)
No abnormality	40(15.38%)
Mass/asymmetry only	110(50%)
Microcalcifications alone	13(5.90%)
Mass with microcalcifications	85(38.63%)
Architectural distortion	12(5.45%)
Ultrasound (n)	N=300
Positive findings	280(93.33%)
No abnormality	20(6.66%)
Mass	270(90%)
Mean tumour size	3.5 cm
NON-mass lesion	10(3.33%)
BI-RADS Category	
1	4(8%)
2	5(1.66%)
3	7(2.33%)
4 (4a-35;4b-124; 4c-91)	210(70%)
5	74(24.66%)

DISCUSSION

According to the last Global Cancer Statistics (GLOBOCAN 2018), breast cancer represented 11.6% of all cancers, which places this disease as the second most commonly diagnosed cancer after lung cancer and caused 6.6% of the total cancer deaths in 2018.⁷ Among women, incidence rates for breast cancer significantly exceeded those for other cancers in both transitioned and transitioning countries, it remaining as a remaining as most commonly diagnosed cancer and the prominent cause of cancer death in women worldwide.⁷

A total of 300 patients who were less than 40 years of age were treated for breast cancer and the mean age was 35.8yrs. 15% patients gave a family history of breast cancer. Of 300 patients, 92.66% were symptomatic. Majority of the patients (52%) presented in III stage at the time of diagnosis. Infiltrating ductal carcinoma (IDC) with or without ductal carcinoma in situ (DCIS) was the most common histopathological diagnosis of breast cancer (91%), followed by pure DCIS in 2.33% and others (invasive lobular carcinoma, papillary carcinoma, medullary carcinoma, lymphoma and adenoid cystic carcinoma) in 6.66%. Of all the IDCs, 69.66% were moderate grade (grade II) and 27% were high grade (grade III). On IHC examinations, ER/PR were positive in 52% of breast tumours with Luminal A (ER/PR positive, Ki-67<14% and HER-2 negative) in 16% & Luminal B HER-2 negative (ER/PR positive, Ki-67≥14% and HER-2 negative) in 44%, Luminal B HER-2 positive (ER/PR and HER-2 positive) in 9.33%, HER-2 enriched (HER-2 positive and ER/PR negative) in 6.3% and triple-negative breast cancer (ER/PR and HER-2 negative) in 47.33% of patients. Digital mammography examinations were performed in 260 of 300 patients with breast cancer as an additional examination to the ultrasound if clinical or sonographic features were suspicious of malignancy or after the pathological diagnosis of malignancy. On digital mammography, breast cancers were suspected in 84.61% patients. Majority of the patients had either heterogeneously dense (ACR type C in 51.92%) or extremely dense (ACR type D in 42.30%) breast tissue. Mass without microcalcifications was detected in 50%, mass with microcalcifications in 38.63%, suspicious microcalcifications alone in 5.90% patients and architectural distortion in 5.45%. False-negative results were observed in 15.38% and all of them had dense breast tissue (ACR type C or type D). Breast ultrasound examinations were

performed in all 300 patients and breast cancers were suspected in 93.33% and false negatives in 6.66% patients. On ultrasound, 90% patients demonstrated mass lesions, and 3.33% patients displayed non-mass lesion with or without ductal calcifications. Majority of the lesions were assigned either BI-RADS 4 (70%) or BI-RADS 5 (24.66%) category. The average tumour size on US was 3.5 cm.

The advantage of detecting the breast lesion early is significant, although it gives people anxiety but prompts them to seek medical advice also earlier.⁸

Sudhir R et al evaluated the characteristic imaging features of breast cancer on mammogram, ultrasound and MRI in women less than 40 years of age and to assess the degree of correlation between clinico-radio-pathological features and biological behaviour. Mammography showed positive findings in 85%, ultrasonography in 94.3% and MRI in 96.4% of women. Majority of the women (69.6%) presented in the late stage (Stage III and IV) with high-grade carcinoma in 39.5% and triple-negative breast cancer (TNBC) in 45.7%. Tumours with HER-2neu expression were associated with the presence of microcalcifications (P-value = 0.006), and TNBC with circumscribed margins or BI-RADS 3/4a category on imaging (P-value = 0.007) and high-grade invasive carcinoma compared to others.⁹

Kuhl et al. showed that sensitivity of mammography, ultrasonography and MRI in asymptomatic women with high risk for breast cancer was 33%, 40% and 91%, respectively.¹⁰

CONCLUSION

The present study concluded that while ultrasound is the recommended imaging method for evaluation of breast under the age of 40 years, we found a better characterization of lesions and higher cancer detection rates when they were also evaluated with mammography.

REFERENCES

1. Sharma, Honey Bhasker, Megha Bansal, and Nikhilesh Kumar. Histomorphological spectrum of neoplastic and non-neoplastic breast lesions—A two-year study in a teaching hospital of North India. *IP Archives of Cytology and Histopathology Research* 3. 4 (2018): 181-4.
2. Jain, Savita Bharat, et al. A clinicopathological study of breast lumps in patients presenting in surgery OPD in a referral hospital in Madhya Pradesh, India. *Int J Current Microbiol App Sci* 4. 8 (2015): 919-23.
3. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185. *CA Cancer J Clin* 2018;68:394-424.
4. Parmar V. Rising incidence of breast cancer in the young fertile Indian population—A reality check. *Indian J Surg Oncol* 2018;9:296-9.
5. Jemal A, Siegel R, Ward E, Hao Y, Xu J, Murray T, et al. Cancer statistics. *CA Cancer J Clin* 2008;58:71-96.
6. Lu J, Steeg PS, Price JE, Krishnamurthy S, Mani SA, Reuben J, Cristofanilli M, Dontu G, Bidaut L, Valero V, Hortobagyi GN. Breast cancer metastasis: challenges and opportunities. 2009: 4951-53.
7. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA: a cancer journal for clinicians*. 2018 Nov;68(6):394-424.
8. Nwafor CC, Udo IA. Histological Characteristics of Breast Lesions in Uyo, Nigeria. *Niger J Surg*. 2018 Jul-Dec;24(2):76-81. doi: 10.4103/njs.NJS_29_17.

9. Sudhir R, Sannapareddy K, Potlapalli A, Penmetsa V. Clinico-radio-pathological features and biological behaviour of breast cancer in young Indian women: A prospective study. *Indian J Radiol Imaging*. 2021 Apr; 31(2): 323–32.
10. Kuhl CK, Schrading S, Leutner CC, Morakkabati-Spitz N, Wardelmann E, Fimmers R, et al. Mammography, breast ultrasound, and magnetic resonance imaging for surveillance of women at high familial risk for breast cancer. *J Clin Oncol* 2005;23:8469-76.