

Histopathological Profile of Breast Cancer and its Association with Sociodemographics and Clinical Characteristics

MANZOOR AHMED¹, VIJAY KUMAR², MUHAMMAD AKRAM³, MUHAMMAD ARSALAN⁴, MOIZ AHMED⁵

¹MBBS, FCPS Fellow Surgery, Jinnah Postgraduate Medical Center Karachi

²MBBS, FCPS Fellow Surgery, Jinnah Postgraduate Medical Center Karachi

³MBBS, FCPS Surgery Resident, Jinnah Postgraduate Medical Center Karachi

⁴MBBS, FCPS Surgery Resident, Bolan Medical College Quetta

⁵MBBS, MO Surgery, Jinnah Postgraduate Medical Center Karachi

Correspondence to: Dr. Vijay Kumar, Email: drvijaybmc@gmail.com, Cell: +923337803555

ABSTRACT

Background: Breast cancer is a heterogeneous disease, though little is known about some of its rarer forms, including certain histologic types. We aim to assess the relationship between the different histologic types of breast cancer and various tumor parameters.

Objectives: To determine the prevalence of histological subtypes of breast cancer and its association with age, molecular subtype, menopausal status, parity, obesity and tumor grade.

Methodology: A prospective, observational study was conducted at Jinnah Postgraduate Medical Center, Karachi, Pakistan from April 2018 to September 2019. The Chi-Square test was used to find the association of histological subtypes with age, molecular subtype, menopausal status, parity, obesity, grade of tumor among breast cancer patients.

Results: We report a prevalence of 91.3% of Invasive Ductal Carcinoma IDC (NOS) among women in our setting. The other rare types of cancer included ILC; 2%, metaplastic 1.4%, and Invasive micropapillary carcinoma; 1%. IDC (NOS) and ILC were significantly associated with luminal A type disease ($p < 0.05$) while metaplastic was associated with basal type disease ($p = 0.006$).

Conclusion: The most prevalent histological subtype of breast carcinoma in our study population was IDC (NOS). However various rarer variants of IDC were also reported. Histological subtypes play a pivotal role in predicting the behavior and clinical outcome of breast carcinomas. The study highlighted our population's demographic and epidemiological variations.

INTRODUCTION

Breast carcinoma is the principal cause of mortality amongst females around the world. ¹ It is estimated that breast cancer accounts for about 400,000 deaths per annum, accounting for 14% of fatalities in women resulting from tumors diagnosed each year. ²⁻⁴ However, these numbers are on the rise; as reported by CDC. ⁵

Breast cancer has an incidence of 14% in females of Pakistan, hence being the most common cancer found in the country. ⁶ In Karachi alone, this cancer accounts for 1/3rd of all malignancies. ⁷ A good prognosis of breast cancer is based on timely detection of the disease, along with an optimized treatment regimen, genetic predisposition to the disease, and numerous other factors. ⁸ Tumors are differentiated based on grades, with grade I being the closest to normal tissue and grade 3 being the most dysplastic, with the least favorable prognosis. ³

Breast cancer is a heterogeneous disease with each variant unique with respect to their clinical characteristics, behavior, and response to treatment regimes, patient survival, and overall prognosis. ⁹⁻¹¹ In this present study, we evaluated the diversity of histological subtypes and assessed the relationship between these subtypes, other clinical parameters and different age groups.

METHODS AND MATERIALS

This was a prospective, observational study conducted at Jinnah Postgraduate Medical Center, Karachi, Pakistan from April 2018 to September 2019. After obtaining ethical approval from the institutional review board of Jinnah Postgraduate Medical Center, study was started. A total of

553 patients with diagnosed cases of breast carcinoma were included in the study. Sample size was calculated using 34.6% ⁶ as the prevalence with 95% Confidence Level. A non-probability, consecutive sampling technique was used to enroll participants in the study. Pregnant patients, metastatic carcinoma of the breast, and those younger than 18 years were excluded from the study.

Data was collected and recorded through a pre defined proforma. Information about the patient's sociodemographics, tumor site, histological subtype, and other parameters were collected by the principal author. Statistical Package for the Social Sciences (SPSS) v.25 was used to run statistical tests on the data collected. The diversity of histological subtypes was presented in tabular and graphical forms. The Chi-Square test was used to find a significant correlation between different histological subtypes, age, menopausal status, parity, obesity, and grades of tumors in breast cancer patients. All continuous variables were presented as mean and standard deviation while categorical/binomial parameters were presented as frequency and percentages. A p-value of < 0.05 was set as statistically significant.

RESULTS

The mean age of participants was 48.25 (10.65) years with 190 (68.6%) patients over the age of forty years and 87 (31.4%) patients under the age of 40 years (Figure 1).

Table 1 demonstrates the histological classification of breast cancer in our study according to the age groups. It was found that invasive ductal carcinoma was the most common histological subtype over all. 76 (84.44%) patients

under 40 years and 159 (83.68%) patients over 40 years had IDC-NOS. The distribution of breast cancer according to histological subtype did not significantly correlate with the age of the patient (p=0.994) (table 1).

The size of the tumor was significantly larger in patients who were over the age of 40 years with a p-value of < 0.001. 132 (69.47%) patients above 40 years had a tumor size of 2-5 cm and 26 (13.68%) had a tumor size of over 5 cm (Table 2).

Nodal metastasis was more significantly common in patients younger than 40 years (p<0.001). 33 (37.93%) patients with N2 stage and 22 (25.29%) patients with N3 stage were younger than 40 years (Table 2).

The majority of the patients who were younger than 40 years had more advanced stage of cancer i.e. 41 (47.13%) patients had stage 3 and 7 (8.05%) had stage IV as compared to those who were older than 40 years (p<0.001) (Table 3 for details).

Age Groups (mean age 48.25 ± 10.65 years)

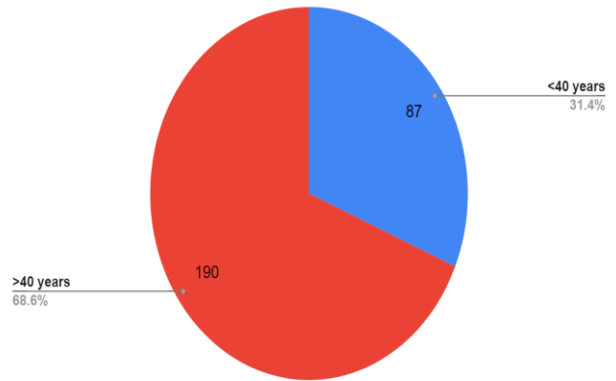


Figure 1. Age Distribution in the Study

Table 1. Histological Classification of Breast Cancer (N = 553)

Histological types	<40 years, n(%)	>40 years, n(%)	p-value
Invasive ductal carcinoma (IDC-NOS)	76 (84.44%)	159 (83.68%)	0.9948
Invasive Lobular Carcinoma (ILC)	7 (7.78%)	16 (8.42%)	
Papillary carcinoma	1 (1.11%)	2 (1.05%)	
Malignant phyllodes	1 (1.11%)	3 (1.58%)	
Medullary carcinoma	3 (3.33%)	4 (2.11%)	
Mucinous carcinoma	1 (1.11%)	3 (1.58%)	
Metaplastic carcinoma	1 (1.11%)	3 (1.58%)	

Table 2. Association of Histological Subtypes & grade of Breast Cancer

Characteristics	<40 years, n(%)	>40 years, n(%)	p-value
Size of the tumor			
Tumor <2 cm (T1)	10 (11.49%)	29 (15.26%)	<0.001
Tumor 2-5 cm (T2)	22 (25.29%)	132 (69.47%)	
Tumor >5 cm (T3)	51 (58.62%)	26 (13.68%)	
Tumor involving chest wall (T4)	4 (4.60%)	3 (1.58%)	
Nodal status			
No lymph node involvement (N0)	11 (12.64%)	47 (24.74%)	<0.001
Metastases to moveable ipsilateral axillary lymph nodes (N1)	21 (24.14%)	82 (43.16%)	
Metastases in ipsilateral axillary lymph nodes that are clinically fixed (N2)	33 (37.93%)	37 (19.47%)	
Metastases that are more extensive (N3)	22 (25.29%)	24 (12.63%)	

Table 3. Stage of Tumor and its Association with Age group

Stages of tumor	<40 years, n(%)	>40 years, n(%)	p-value
Stage I	9 (10.34%)	29 (15.26%)	<0.001
Stage II	30 (34.48%)	121 (63.68%)	
Stage III	41 (47.13%)	35 (18.42%)	
Stage IV	7 (8.05%)	5 (2.63%)	

DISCUSSION

According to the WHO, there are over 20 histological subtypes of breast carcinoma. Out of these, IDC is the most common type, with a global prevalence of 40-70%⁷. These diverse subtypes differ significantly with respect to their behavior, hence, affecting the prognosis and response to therapy⁸⁻⁹. Each of the subtypes of breast cancer influence the clinical behavior, survival outcome, the

response to therapy and eventually the quality of life of the survivors.¹⁰⁻¹¹

In the current study, over 550 diagnosed cases of breast carcinoma were analyzed. The mean age of patients was 46.75 + 10.85 years. 56 (10.1%) patients were younger than 35 years 318 (57.5%) were in between 35 to 50 years of age, while 179 (32.4%) were older than 50 years.

Multiple studies have indicated an identical age pattern for women belonging to Asian countries such India and Pakistan. These studies have shown that women belonging to these regions have a younger age of presentation. In comparing breast cancer among Pakistanis and Caucasians, it was revealed that 16.2% women with breast cancer were below the age of 40 in Pakistan, as compared to 6.23% of caucasians belonging to the same age group ($p < 0.0001$).¹¹⁻¹⁵

Our study included a majority of premenopausal women, which may indicate an association with risk factors such as diet, carcinogens or pollution. These factors may result in a younger age of presentation. Though nulliparous and obese women are at a significant risk of developing breast cancers, our study included a majority of parous women but with a normal BMI.

On evaluation of several subtypes we found in our study, IDC-NOS was the most dominant form of breast cancer. However, some rare kinds of breast cancer were also reported in our study. The results of our study were similar to a study conducted in the city of Karachi by Aga Khan University Hospital in the year 2000. The study reported 81.99%, 2% and 1.4% prevalence of IDC, ILC and metaplastic subtype respectively [13]. In the same year, it was found that ductal carcinoma in situ had a prevalence of 16.25%, making it the second most common type of breast tumor. This was followed by mucinous carcinoma, infiltrating lobular carcinoma and papillary carcinoma, which had the prevalence of 0.52%, 0.34% and 0.17% accordingly. Another study conducted in the year 2017 also reported that 84.8% of the patients evaluated had IDC, belonging to the age group of over 60 years.¹⁴

A similar study conducted by Khokher studied the histological subtypes of breast cancer among women in a local cancer hospital in Pakistan. The findings revealed that of the patients evaluated, 4% had an unknown histological type, which 91%, 2% and 1% were classified as invasive ductal carcinoma, invasive lobular carcinoma and mucinous carcinoma respectively.¹⁵ These findings supported our study, which also highlighted invasive ductal carcinoma as the most common breast carcinoma in women. Women may have a higher prevalence of IDC than ILC due to reasons such as a variable risk profile. The study also revealed an advanced stage of cancer at presentation, which was also found in our study, this implies that females may have a lack of access to mammography machines and there may be an absence of screening programs in the country.

In the developed world, the most common age of presentation is 60 to 70 years while in developing countries such as Pakistan peak age is 40-50 years.¹⁶ Naeem et al., found that the most common age group of Pakistani women presenting with tumors was between 40-49 years.¹⁷ This was also revealed in our study, where 57.5% of the

population belonged to the age group of 35 to 40 years. In Pakistan, younger presentation may be due to a considerably younger age structure and shorter life expectancy among women.¹⁵

CONCLUSION

The most prevalent histological subtype of breast carcinoma in our study population was IDC (NOS). However various rarer variants of IDC were also reported. Histological subtypes play a pivotal role in predicting the behavior and clinical outcome of breast carcinomas. The study highlighted our population's demographic and epidemiological variations.

REFERENCES

1. Akram M, Iqbal M, Daniyal M, Khan AU. Awareness and current knowledge of breast cancer. *Biological research*. 2017 Dec;50(1):1-23.
2. Baquet CR, Commiskey P. Socioeconomic factors and breast carcinoma in multicultural women. *Cancer*. 2000 Mar 1;88(S5):1256-64.
3. Li T, Mello-Thoms C, Brennan PC. Descriptive epidemiology of breast cancer in China: incidence, mortality, survival and prevalence. *Breast cancer research and treatment*. 2016 Oct;159(3):395-406.
4. Nguyen DN, Simms K, Nguyen HQ, Van Tran T, Nguyen NH, LaMontagne DS, Castle P, Canfell K. The burden of cervical cancer in Vietnam: Synthesis of the evidence. *Cancer epidemiology*. 2019 Apr 1;59:83-103.
5. Coughlin SS, Ekwueme DU. Breast cancer as a global health concern. *Cancer epidemiology*. 2009 Nov 1;33(5):315-8.
6. Badar F, Mahmood S, Faraz R, Yousaf A, Quader AU, Asif H. Epidemiology of breast cancer at the Shaukat Khanum memorial cancer hospital and research center, Lahore, Pakistan. *J Coll Physicians Surg Pak*. 2015 Oct 1;25(10):738-42.
7. Bhurgri Y, Kayani N, Faridi N, Pervez S, Usman A, Bhurgri H, Malik J, Bashir I, Bhurgri A, Hasan SH, Zaidi SH. Patho-epidemiology of Breast Cancer in Karachi 1995-1997. *Asian Pacific Journal of Cancer Prevention*. 2007 Apr 1;8(2):215.
8. Osuch JR, Bonham VL. The timely diagnosis of breast cancer: principles of risk management for primary care providers and surgeons. *Cancer*. 1994 Jan;74(S1):271-8.
9. Beg S, Haider G, Khan E, Shahid A, Memon P, Rahul R, Pawan B, Abbas K. DIVERSITY OF HISTOLOGICAL VARIANTS OF BREAST CANCER: A TERTIARY CARE HOSPITAL EXPERIENCE IN KARACHI, PAKISTAN. *Pakistan Armed Forces Medical Journal*. 2020 Aug 20;70(4):1119-24.
10. Khan ME, Haider G, Ahmed K, Ahmed M, Manzoor A, Masood A, Shaikh S, Abbas K. Ethnic differences in the receptors status of estrogen, progesterone and Her2/Neu among breast cancer women: A single institution experience. *JPMA*. 2020;70(1970).
11. Ahmed M, Mahmood N, Zaffar S, Rafique U, Ahmed M, Abbas K. IMPACT OF BREAST CONSERVATION SURGERY VERSUS THE MODIFIED RADICAL MASTECTOMY ON THE QUALITY OF LIFE AMONG BREAST CANCER SURVIVORS IN PAKISTAN. *Pakistan Armed Forces Medical Journal*. 2020 Dec 16;70(6):1815-9.
12. Rahool R, Haider G, Hayat M, Shaikh MR, Memon P, Pawan B, Abbas K. Factors Associated With Treatment Delay in Breast Cancer: A Prospective Study. *Cureus*. 2021 Feb 9;13(2).
13. Siddiqui MS, Kayani N, Sulaiman S, Hussainy AS, Shah SH, Muzaffar S. Breast carcinoma in Pakistani females: a morphological study of 572 breast specimens. *Journal-Pakistan Medical Association*. 2000 Jun;50(6):174-6.
14. Shams MU, Riaz S, Amjad U, Aamir Z. Histopathological Features of Breast Carcinoma in Post Menopausal Women (60 Years and Above): Five Years Experience at a Teaching Hospital in Pakistan. *Proceeding SZPGMI Vol*. 2017;31(1):19-22.
15. Khokher S, Qureshi MU, Riaz M, Akhtar N, Saleem A. Clinicopathologic profile of breast cancer patients in Pakistan: ten years data of a local cancer hospital. *Asian Pac J Cancer Prev*. 2012 Jan 1;13(2):693-8.
16. Leong SP, Shen ZZ, Liu TJ, Agarwal G, Tajima T, Paik NS, Sandelin K, Derossis A, Cody H, Foulkes WD. Is breast cancer the same disease in Asian and Western countries?. *World journal of surgery*. 2010 Oct 1;34(10):2308-24.
17. Naeem M, Khan N, Aman Z, Nasir A, Samad A, Khattak A. Pattern of breast cancer: experience at Lady Reading Hospital, Peshawar. *J Ayub Med Coll Abbottabad*. 2008 Dec 1;20(4):22-5.