

Frequency and Pathologic Features of Triple Negative Breast Cancer at A Tertiary Care Hospital in Pakistan

Khurram Shehzad¹, Sadia Alam², Muhammad Usman Shams³, Sabiha Riaz⁴, Haseeb Ahmed Khan⁵, Rizwan Ullah Khan⁶

- 1 Resident Doctor, Department of Pathology, FMH College of Medicine & Dentistry, Lahore Pakistan
Conception & designing, Acquisition of data, Writing manuscript & final approval
- 2 Resident Doctor, Department of Pathology, FMH College of Medicine & Dentistry, Lahore Pakistan
Conception & designing, Acquisition of data, Critical evaluation, Writing manuscript & final approval
- 3 Assistant Professor, Department of Pathology, FMH College of Medicine & Dentistry, Lahore Pakistan
Acquisition of data, Revision of manuscript & final approval
- 4 Professor, Department of Pathology, FMH College of Medicine & Dentistry, Lahore Pakistan
Acquisition of data, Drafting the manuscript & final approval
- 5 Assistant Professor, Department of Pathology, FMH College of Medicine & Dentistry, Lahore Pakistan
Acquisition of data, Drafting the manuscript & final approval
- 6 Assistant Professor, Department of Pathology, FMH College of Medicine & Dentistry, Lahore Pakistan
Acquisition of data, Drafting the manuscript & final approval

CORRESPONDING AUTHOR

Dr. Haseeb Ahmed Khan

Assistant Professor, Department of Pathology, FMH College of Medicine & Dentistry, Lahore Pakistan
Email: haseeb.a.khan@hotmail.com

Submitted for Publication: 01-03-2021
Accepted for Publication 12-06-2021

How to Cite: Khurram Shehzad, Sadia Alam, Muhammad Usman Shams, Sabiha Riaz, Haseeb Ahmed Khan, Rizwan Ullah Khan. Frequency and Pathologic Features of Triple Negative Breast Cancer at A Tertiary Care Hospital in Pakistan. APMC 2021;15(2):136-8. DOI: 10.29054/APMC/2021.1160

ABSTRACT

Background: Triple negative breast cancers (TNBC) are a subtype in the molecular classification of breast cancers and are defined by lack of expression of ER, PR and HER2. TNBCs show aggressive behavior, rapid growth, shorter survival & propensity for distant metastasis. **Objective:** This study was conducted to see the frequency and pathologic features of TNBC in our population to help in better understanding of this aggressive disease in Pakistani women. **Study Design:** Retrospective study. **Settings:** Department of Pathology, Fatima Memorial Hospital, Lahore Pakistan. **Duration:** January 2011 to August 2016. **Methodology:** All the breast cancer cases in which immunohistochemistry for ER, PR and Her2 was performed at the Department of Pathology, Fatima Memorial Hospital (Lahore) from January 2011 to August 2016 were reviewed. TNBC cases were identified and the data was analyzed. **Results:** Out of total 246 breast cancer cases on which receptor studies were done, 46 (18.7%) cases of TNBC were identified. 71% of these cases were in women below the age of 50 years. The cancer involved right breast in 24 (52.1%) cases and left breast in 18 (39.1%) cases. 41 (89.1%) cases were invasive ductal carcinoma. 20 (43.5%) were grade 2 and 26 (56.5%) were grade 3. **Conclusion:** Frequency of TNBC in Pakistani population is 18.7% and it is affecting younger age females usually below 50 years of age.

Keywords: Breast cancer, TNBC, Triple negative, Immunohistochemistry, Histopathology.

INTRODUCTION

Breast cancer is one of the most common malignancies worldwide. It constitutes 23% of all cancer patients and accounts for 14% of cancer related deaths.¹ The incidence of breast cancer has increased in past decades in Asian continent and Pakistan has the highest prevalence of breast cancer within Asia.²

Breast cancer is a heterogeneous disease with various subtypes having distinct and diverse clinical presentation, prognosis, histological features and therapeutic response to treatment modalities. This heterogeneity has led to various subtyping schemes time to time with molecular classification of breast cancer being the latest.³ It is based on the molecular evidence of different pathways leading to the development of invasive breast cancers.⁴

Triple negative breast cancer (TNBC), one of the subtypes in the molecular classification of breast cancers is defined

by lack of expression of ER, PR and HER2. It accounts for 12-17% of all breast cancers with special predilection for African- American descent. These cancers present in an earlier age with risk specially increased before the age of 50 years.⁵

TNBC & basal like breast cancer terminologies have been used interchangeably very often but these are not essentially similar entities. 50 to 80% TNBCs are basal like breast cancers but basal like breast cancer is a molecularly defined category of breast cancer with expression of certain specific set of genes like EGFR, CK5/6 & proliferation gene clusters. The basal like breast cancer also have low expression of hormone receptor and HER2 gene and thus all basal like breast cancers are not TNBCs.^{6,7}

Similarly, TNBCs represent a heterogeneous group at the molecular level by gene expression studies. Most of TNBCs are associated with molecular classes including

basal like, claudin low and molecular apocrine group. Majority of the TNBCs are of invasive ductal carcinomas, No special type. They represent certain histological features like high nuclear grade, pushing borders, central necrosis, brisk lymphocytic infiltration and increased mitosis.

Special histological subtypes with triple negative phenotype are metaplastic carcinomas, salivary gland type neoplasms, carcinomas with apocrine features & carcinomas with medullary features.^{8,9}

TNBCs show aggressive behavior, rapid growth, shorter survival & propensity for distant metastasis. There is increased rate of local and distant relapse with visceral or brain metastasis. The five-year recurrence rate is approximately 30%.^{10,11,12}

As TNBCs do not express hormone and HER2 receptors, so endocrine and anti-Her2 therapy does not benefit these patients. They are treated with chemotherapy, however several molecular based therapies with target specific biomarkers are being developed. These biomarkers include EGFR targeted agents, androgen receptor agents, anti-antigenic agents and PARP inhibitors.^{13,14} Purpose of our study is to see the frequency of TNBC in our population so that the trends, behavior, therapeutic response of TNBC can be better understood in Pakistani population. It will help us in improving the survival, evaluation of prognosis and provide a basis for development of new and better treatment options.

METHODOLOGY

Study Design: Retrospective study.

Settings: Fatima Memorial Hospital, Lahore Pakistan.

Duration: January 2011 to August 2016.

Sample Size: 246 cases of primary breast cancers.

Inclusion Criteria: All female patients with diagnosed invasive carcinoma of breast on the basis of histopathology were included in the study.

Exclusion Criteria: Poorly preserved, post treatment/post chemotherapy cases of breast cancers were excluded from the study.

Data Collection Procedure: Immuno-histochemical stains ER, PR and HER2 were performed on these cases and results were recorded accordingly. Clinico-pathological parameters including age, tumor type, histological subtype, and staging were evaluated. Histological grades were assessed in accordance with standard guidelines. Results of ER, PR and Her2 were assessed on the basis of College of American Pathologists guidelines. Any tumor with less than 1% immunoreactive cells was considered negative for ER and PR stains. Her2 stain was considered negative when no staining was observed or membrane staining that was incomplete and faint/barely perceptible and within $\leq 10\%$ of tumor cells, or incomplete membrane staining that was faint/barely perceptible and within $>10\%$ of tumor cells.

RESULTS

Total number of breast cancer cases included in study were 246. 46 (18.7%) cases were ER, PR and Her2 negative and thus fell in the category of triple negative breast cancers. 71% of these cases were in women below the age of 50. the cancer involved right breast in 24 (52.1%) cases and left breast in 18 (39.1%) cases. Out of total 46 cases, invasive ductal carcinoma (IDC) were diagnosed in 41 (89.1%) cases. 4 cases were diagnosed as mixed carcinoma. One case of metaplastic carcinoma was diagnosed. Regarding histological grade, 20(43.5%) cases were of grade 2 and 26 (56.5%) cases were of grade 3. Among 6 cases with available T staging data, pT2, pT3 and pT4 cases were 2, 1 and 3 respectively. Pathological N staging was available in 4 cases which showed 2, 1 and 1 case of pN0, pN2a and pN3a respectively.

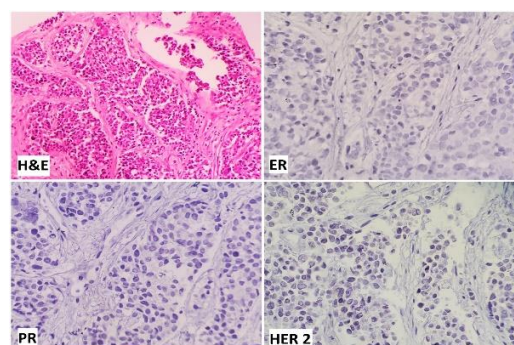
Table 1: Age distribution of TNBC cases

Age Range (years)	No. of cases	%
21-30	04	8.69
31-40	08	17.39
41-50	19	41.30
51-60	05	10.86
Above 60	10	21.74

Table 2: Pathologic features of TNBC cases

Features		No. of cases	Percentage %
Frequency		46	18.7%
Histological type	IDC	41	89.13%
	Mixed carcinoma	4	8.69%
	Metaplastic carcinoma	1	2.17%
Histologic grade	Grade 1	0	0%
	Grade 2	20	43%
	Grade 3	26	57%
Laterality	Right	24	52.17%
	Left	18	39.13%
	Not specified	26	8.69%
Pathological staging	pT2	2	33.33%
	pT3	1	16.66%
	pT4	3	50%

Figure 1: Breast carcinoma, H&E (100x); ER negative (200x); PR negative (200x); Her2 negative (200x)



DISCUSSION

Breast cancer is disease of high significance in Pakistan with incidence of 21.5% in all & 45.9% among females. Approximately 12-17% of breast cancer cases are of TNBC. In our study, the frequency of TNBC in Pakistani population is 18.7% that coincides with the results of other studies.¹⁴⁻¹⁶ Another study done by Hashmi et al shows the frequency of TNBC in Pakistani population as 15.5%.⁷ Frequency of TNBC in an Indonesian study accounted for 25% cases.¹⁷ 12.2% and 13% TNBC cases were reported in Kuwait and Singapore respectively.^{18,19} TNBC is most frequently seen in young and premenopausal women as compared to other breast cancer subtypes.^{20,21} Similar results were seen in our study with 71% of cases involving women below the age of 50 years. It is also comparable to other study from Pakistan with 70% of cases having age less than 50 years. Invasive ductal carcinoma, no special type was the most common subtype encountered in our study. It is concordant to the findings of other studies which show the most common histological subtype of TNBC as invasive ductal carcinoma, no special type with higher grade histology.

The histological grade was grade II and grade III in 43.5% & 56.5% respectively, represent the similar results with TNBCs worldwide. Japanese study by Kutoni G, et al.^{8,9,22,23} and study by Akhtar M et al done in India also have the same results.

In our study, most common involvement of the right breast was seen and it coincides with a study done by Fayyaz MS et al in Kuwait.¹⁸ Pathological staging was higher in our study which is seen to be associated with this phenotype of breast cancer. Thus, our results are in accordance with other studies.¹³

CONCLUSION

The frequency of triple negative breast cancer is 18.7% in Pakistani population. Keeping in view the aggressive behavior, frequent recurrences, poor survival rate and limited therapeutic options, extensive work is required for development of targeted therapies for treating these cancers and to have better prognosis and survival for the patients.

CONFLICT OF INTEREST / DISCLOSURE

None to declare.

REFERENCES

- Eliyatkina N, Yalcin E, Vardar E. Molecular classification of breast carcinoma from traditional, old-fashioned way to a new age and a new way. *J Breast Health*. 2015;11(2):59-66.
- Najafi B, Anvanan S, Roshan ZA. Disease for survival among molecular subtypes of early-stage breast cancer between 2001 and 2010 in Iran. *Asian Pac J cancer prev*. 2013;14(10):5811-16.
- Akbar M, Akbar K, Naveed D. Frequency and correlation of molecular subtypes of breast cancer with clinicopathological features. *J Ayub Med Coll Abbottabad*. 2014;26(3).
- Allison KH. Molecular pathway of breast cancer. What a pathologist needs to know. *Am J of Clin Pathol*. 2012;770-80.
- Kozakiewicz AM, Budzik MP, Liszc A, Sobieraj MT, Czerw AL, Sobol M, et al. Clinicopathological factors associated with novel prognostic markers for patients with triple negative breast cancer. *Arch Med Sci*. 2019;15(6):1433-42.
- Stovgaard ES, Nielsen D, Hogdall E, Balslev E. Triple negative breast cancer, prognostic role of immune related factors, a systemic review. *Acta oncol*. 2018;57(1):74-82.
- Hashmi AA, Edhi MM, Naqvi H, Faridi N, Khurshid A, Khan M. Clinicopathologic features of triple negative breast cancer, an experience from Pakistan. *Diagn Pathol*. 2014;9:43.
- Elsa Z, Sinr HP. Triple negative breast cancer, clinical and histological correlation. *Breast Care*. 2011;6(4):273-78.
- Pareja F, Geyer FC, Mecchio C, Burke KA, Weigelt B, Filho JS. Triple negative breast cancer: The importance of molecular histologic subtyping and recognition of low grade variants. *NPJ Breast Cancer*. 2016;2:16036.
- Ring BZ, Hout DR, Morris SW, Lawrence K, Schweitzer BL, Bailey DB, et al. Generation of an algorithm based as gene sets to clinically subtype triple negative breast cancer patients. *BMC cancer*. 2016;16:143.
- Albergaria A, Ricardo S, Milanezi F, Carneiro V, Amendoeira I, Vieira D, et al. Nottingham prognostic index in triple negative breast cancer, a group of breast cancer with aggressive behavior. *BMC cancer*. 2011;11:299.
- Collignon J, Lousberg L, Schroeder H, Jerusalem G. Triple negative breast cancer: treatment challenges and solutions. *Breast cancer*. 2016;8:93-107.
- Aysola K, Desai A, Welch C, Xu J, Qin Y, Reddy V, et al. Triple negative breast cancer, an overview. *Hereditary genet*. 2013(2):001.
- Yeh J, Chun J, Schwartz S, Wang A, Kern E, Guth AA, et al. Clinical characteristics in patients with triple negative breast cancer. *International journal of breast cancer*. 2017.
- Shaukat U, Ismail M, Mahmood N. Epidemiology, risk factors and genetic predisposition for breast cancer in the Pakistani population. *Asian Pac J Prev*. 2013;14(10):5625-9.
- Boyle P. Triple negative breast cancer epidemiological considerations and recommendations. *Ann Oncol*. 2012;23:7-12.
- Widodo J, Dwianingsih EK, Triningsih E, Utoro T, Soeripto, et al. Clinicopathological features of Indonesian breast cancers with different molecular subtypes. *Asian Pac J of can prev*. 2014;15:6109-113.
- Fayyaz MS, EL-Sherify MS, EL-Basmy A, Zlouf SA, Nazmy N, George T, et al. Clinicopathological features and prognosis of triple negative breast cancer in Kuwait. *Rep Pract oncol radiother*. 2014;19(3):173-81.
- Thike AA, Cheok PY, Jara-Lazaro AR, Tan B, Patrick Tan P, Tan PY, et al. Triple-negative breast cancer, clinicopathological characteristics and relationship with basal-like breast cancer. *Mod Pathol*. 2010;23:123-33.
- Couch FJ, Hart SN, Sharma P, Toland AE, Wang X, Miron P, et al. Inherited mutations in 17 breast cancer susceptibility genes among a large triple negative breast cancer cohort unselected for family history breastcancer. *J clin onco*. 2015;3(4):304-11.
- Sandhu GS, Ergou S, Patterson H, Mathew A. Prevalence of triple negative breast cancer in India. *J Glob oncol*. 2016;2(6):412-21.
- Kutoni G, Ohmura T, Suzuki Y, Kameshima H, Shima H, Takamaru T, et al. Clinicopathological characteristics of triple negative breast cancer. 2012;3:836.
- Akhtar M, Dasgupta S, Rangwala M. Triple negative breast cancer: an Indian perspective. *Breast cancer: target and therapy*. 2015;7:293-43.