Original Article

Carcinoma Breast

Frequency of Triple Negative Receptor Status in Patients Diagnosed with Carcinoma Breast

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ABSTRACT

Objective: To determine the frequency of triple negative receptor status in patients diagnosed with carcinoma breast.

Study Design: Descriptive / cross sectional study.

Place and Duration of Study: This study was conducted at the Department of Surgical Unit III of Nishtar hospital, Multan from July 2016 to December 2016.

Materials and Methods: A total of one hundred and seventy one female patients of age between 30-60 years who were diagnosed breast cancer were presented in this study. All numerical variables were presented as mean ± standard deviation and categorical variables were presented as frequency and percentages. Chi square test was applied to see the effect of confounders. $P \leq 0.05$ was considered as significant.

Results: It was noted that out of 100% (n=171) patients, 20.5% (n=35) were having TNBC and 79.5% (n=136) were not. It was also observed that out of these 100% (n=171) patients, a big majority 78.9% (n=135) were having Menopausal Status and 21.1% (n=36) were not. While Family History of TNBC showed that 18.1% (n=31) were Positive TNBC. Out of these 100% (n=171) patients, a big majority 78.9% (n=135) were having Menopausal Status. While Family History of TNBC showed that 18.1% (n=31) patients with positive family history were having Positive TNBC.

While, the incidence of SSI in group B (without SD) was 20% (14/70) and 4% (03/70) in group A (with SD). Anastomosis leak was observed only in B group. The median post-operative hospital stay was 14 (range, 9-42 days) in B group and 12 days (range, 8-27 days) in group A. There were hospital re-admission in 03 patients of B group, with no mortality in any group. However, the incidence of SSIs when comparing both groups (group B versus group A), did reach statical significance of $P < 0.38$.

Conclusion: Breast cancer particularly triple negative disease was found in younger age group and patients usually present in advanced stage of their disease.

Key Words: Triple negative breast cancer, Ductal carcinoma in situ, Carcinoma breast, Metastasis

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INTRODUCTION

Breast cancer is a leading cause of death in women, worldwide, it is most often diagnosed life threatening incident in female[1]. In United States breast cancer found 29% of all cancers which holds 2nd rank after lung cancer as a cause of death[2]. Due to its severity and proliferation surgery has been recommended as a primary treatment. Lot of patients with early stage of breast cancer is cured with surgery alone without chemotherapy and radiotherapy.

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Breast cancer is a heterogeneous disease by its molecular and genetic studies and can be classified into different groups on the basis of its immune histochemical biomarkers [3] such as progesterone receptors, estrogen receptors and human epidermal growth factor receptors 2 are the leading ones [4,5]. In 2007 St. Gallen proposed a combination therapy also known as adjuvant therapy (chemotherapy, endocrine therapy, and trastuzumab) for the treatment of primary breast cancer labeled on the basis of estrogen receptors (ER), progesterone receptor (PR) and human epidermal growth factor receptor 2 (HER2)[6].

Another subtype of breast cancer known as triple negative breast cancer (TNBC) that was negative for PR, ER and HER2 is found to be most difficult to treat among these newly classified breast cancers. The main cause of difficulty in its treatment is unavailability of targeted therapy such as lapatinib, trastuzamab and ER modulators. Metastatic property of TNBC is similar to other subtypes but it takes shorter time periode to proliferate and death. Frequency of TNBC found between 10-20 % of all breast cancers and mostly

diagnosed in young premenopausal female with more aggressive biological feature and higher proliferation rate. Globally, frequency of breast cancer varies according to the geographic changes, genetic variations, environmental factors and living status 8: as found in Mozambique 3.9/100,000 and in U.S 101.1/100,000.[7]

Patil VW et al.[8] conducted a study on triple neative breast cancer in Indian population with sample size of 683 patients and found frequency of positive TNBC (Negative for Estrogen receptor, Progesterone receptor and her-2/neu receptor) in 136 (19.92%) of patients and neative TNBC in 529 (77.45%) of patients. They also concluded that TN breast cancer was found mostly in younger age (<35 years)[9, 10]. In another study conducted by Ambroise M[11] frequency of TNBC was found in 25% of patients. But, we could not find any study conducted to investigate the frequency of TNBC in Pakistani population. After this study we will be able to find out the frequency of triple negative breast cancer TNBC status in our local patients, purpose of this study is not only to add local information in our database but also to pay attention to this aggressive disease by routine screening and close monitoring of cancer patients.

MATERIALS AND METHODS

This cross sectional descriptive study was conducted on female patients of age between 30-60 years who were diagnosed breast cancer. After approval from ethical review committee of hospital, a total of 171 patients were enrolled during period of July 2016 to December 2016 in department of Surgical Unit III of Nishtar hospital, Multan. Sample size was calculated from formula ($n = z^2 \times p (1-p) / d^2$), z = 1.96. p = 19.92% (Anticipated proportion of patients with Triple negative receptor status) and d = 6%. Carcinoma Breast was diagnosed on the basis of history and clinical examination with a lump in the breast and was confirmed on histopathology of the breast lump. Triple negative receptor status was labeled to be present if the histopathological specimen turns out to be negative for Estrogen receptor, Progesterone receptor and Her/neu receptor on immune-histochemistry from an aunthentic laboratory (Shaukat Khanam Memorial Trust Hospital). It was labeled to be absent if any of the three receptors were found to be present in the histopathological specimen on immunohistochemistry. Each patient was assured for maintaining privacy and confidentiality and that the name of the patient was not be disclosed in the results. Study protocol, use of data for research and risk-benefit ratio was explained to each patient to take an informed and understood consent. The demographic information like name and age were recorded. All these patients were undergo mastectomy by Consultant surgeon (having 5 years' post-fellowship experience). All the specimens were sent to a reference laboratory(Shaukat Khanam Memorial Trust Hospital) for immune staining for presence or absence of Esterogen receptor, Progesterone receptor and Her / neu receptor. All this data was noted on a structured proforma (Annexure).Patients unfit to undergo surgical excision, established metastatic disease and irregular menstrual cycle were excluded.

The data was analyzed using SPSS version 19.0. Mean and standard deviation was calculated for quantitative variables like age and size of the tumor. Frequency and percentages were calculated for qualitative variables like triple negative receptor status (present/ absent). Effect modifier like age and size of the tumor was controlled through stratification and post-stratification chi square was applied to see the effect of these on outcomes. P-value of ≤ 0.05 was taken as statistically significant.

RESULTS

A total of 171 patients were included in this study (all were female). The mean age of the patients was 43.46 ± 8.38. The mean size of tumor of the patients was 2.52 ± 0.025. The main outcome variable of this study was the Triple negative receptor status (TNBC). In our study it was noted that out of 100% (n=171) patients, 20.5% (n=35) were having TNBC and 79.5% (n=136) were not. It was also observed that out of these 100% (n=171) patients, a big majority 78.9% (n=135) were having Menopausal Status and 21.1% (n=36) were not. While Family History of TNBC showed that 18.1% (n=31) patients with positive family history were having Positive TNBC and 81.9% (n=140) were not.

These 100% (n=171) patients were divided into three groups with respect to age categories i.e. patients from 30-40 years included in group 1, including 38.6% (n=66) patients, aged from 41-50 years included in group 2, including 40.4 (n=69) patients, and patients from 51-60 years of age included in group 3, including 21.1% (n=36) patients.

When chi-square was applied to check the effect modification it was observed that family history and stratified age were significantly associated with TNBC having P-values 0.033 and 0.000 respectively. And in our study, Menopausal Status was not significantly associated with TNBC with P-value 0.769.

Table No.1: Demographics (n=171)

Characteristics	Frequency	Percentage (%)
TNBC		
Yes	35	20.5
No	136	79.5
Total	171	100.0
Menopausal Status		
Yes	135	78.9
No	36	21.1
Total	171	100
Family History		
Yes	31	18.1

No	140	81.9
Total	171	100
Stratified Age		
30-40 years	66	38.6
41-50 years	69	40.4
51-60 years	36	21.1
Total	171	100

Table-2: TNBC with respect to Menopausal Status

Menopausal Status	TNBC		Total
	No	Yes	
No	28	8	0.769
Yes	108	27	
Total	136	35	

Table-3: TNBC with respect to Family History

Family History	TNBC		Total
	No	Yes	
No	107	33	0.033
Yes	29	2	
Total	136	35	

DISCUSSION

Breast cancer is a heterogeneous disease when assessed on clinical, pathological and molecular basis[12]. In earlier times it was classified by size due to limited knowledge about this disease. But now in these days with the help of histological knowledge breast cancer was divided into eighteen subtypes. A common subtype of cancer ductal carcinoma cannot be classified without histological involvement. This histomorphological classification of BC is also not capable to design homogenous groups for treatment options. This heterogeneous nature of cancer is a challenge for physicians and patients to treat as treatment modalities are not directed towards targeted therapy.When gene expression profiling came into existence than breast cancer was classified into five distinct gene expression profiles based subtypes by cDNA microarray analysis, on basis of this classification treatment modalities were started. Among these five subtypes three are derived from ER tumors and two are derived from ER+ subtypes also known as luminal "a" and b[13]. Other than these two types another type of breast cancer exits known as triple negative breast cancer TNBC, found 10-17% of all breast cancers.

In our study total of one hundred and seventy six patients were included (all were female). The mean age of the patients was 43.46 ± 8.38. The main outcome variable of this study was the Triple negative receptor status (TNBC) and it was found that out of 100% (n=171) patients, 20.5% (n=35) were having TNBC and 79.5% (n=136) were not. In a study conducted by Khan RI et al.[14] on Pakistani population, pathological record of 4715 samples was analyzed. TNBC was found in 815 (17.2%) patients. This percentage of TNBC was closer to upper margin of the range investigated globally. In this study mean age of TNBC positive patients was 46.26 ± 12.22 years which is significantly younger than that global figure. These results were comparable with our results. In a study conducted by Sajid MT [15]at Women College Hospital and University, Toronto, Canada, incidence of TNBC was 11.2% with mean age of <53 years. A large number of patients about 90% were TNBC found within basal like subtype as named according to its gene expression. This type of BC mostly found in African and American population [111].

In a study conducted by Sajid M and Ahmad M[15]on age related frequency of triple negative breast cancer in women and reported thatTNBC was found in 17.28% of the Pakistani female who were diagnosed breast cancers. Out of TNBC positive patients, 537 patients (65.88%) were aged < 50 years while 278 (34.11%) patients were aged > 50 years. (*p < 0.001*). A large number of patients were fall within younger age group. Involvement of younger patients requires more attention for treatment invention and management of TNBC. The results of our study are near about to this study and comparable.

In a study conducted by Marwan G et al.[16]data analysis was done on 1, 834 patients out of them in 9.3% patients TNBC was found median age of these patients was 52 years. He further divided these patients in subgroups as positive family history was reported in 15 (9%) patients, invasive ductal carcinaoma reported as 85%, medullary carcinoma reported as in 5%, invasive lobular carcinoma was in 5% of triple negative breast cancer patients. This study has small percentage of TNBC as compared to many previous studies.In our study it was also observed that out of these 100% (n=171) patients, a big majority 78.9% (n=135) were having Menopausal Status and 21.1% (n=36) were not. While Family History of TNBC showed that 18.1% (n=31) were Positive TNBC and 81.9% (n=140) were not. The mean size of tumor of the patients was 2.52± 0.025. Similarly, in a study conducted by Tanja O et al.[17]reported that a large number of patients were postmenopausal (60.3%) when presented at center of enrollment mostly patients were fall in grade III category (82.5%), in this study 59% of patients were having tumor size more than 2 cm.

Thike A et al.[18] conducted a study on ductal carcinoma in situ associated with triple negative invasive breast cancer: evidence for a precursor-product relationship and reported 97.9% triple negative which include oestrogen receptor, progesterone receptor and cerbB2 negative. In some previous studies conducted by Gluz O [19], Dawson SJ [20], Elston CW [21] it is reported that triple negative breast cancers were comparatively of lager size (>2cm) than other cancers.

CONCLUSION

Breast cancer particularly triple negative disease was found in younger age group and patients usually present in advanced stage of their disease.

Conflict of Interest: The study has no conflict of interest to declare by any author.

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