DOI: https://doi.org/10.53350/pjmhs22162530

**ORIGINAL ARTICLE**

# Triple Negative Receptor Status in Patients Diagnosed with Carcinoma Breast

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## ABSTRACT

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

**Methodology:** This descriptive cross-sectional survey, was conducted at Surgical Unit III, Nishtar Hospital Multan, we included 171 females between 30-60 years of age diagnosed to have breast carcinoma on histopathology whereas those unfit to undergo surgical excision, established metastatic disease were excluded from the study. All these patients were undergo mastectomy by Consultant surgeon (having 5 years' post-fellowship experience). All the specimens were sent to areference laboratory(Shaukat Khanam Memorial Trust Hospital) for immune staining for presence or absence of Esterogen receptor, Progesterone receptor and Her / neu receptor. Frequency was calculated for triple negativereceptor status (present/absent).

**Results:** Total patients included in this study were 171 (100%) all were female. These 171 patients were divided into 3 groups, patients from 30-40 years included in group 1, age 41-50 included in group 2 and patients from 51-60 years included in group 3. According to age patients in which TNBC was present were have mean age 44.06 and standard deviation 9.107 similarly patients in which TNBC was absent were have mean age of 44.32 and standard deviation 8.953. According to TNBC patients of group 1 (30-40 years), 13 were have TNBC present and 53 were not, out of 55 patients of group 2 (41-50 years), 12 were have TNBC present and 43 were not, similarly out of 50 patients in group 3 (51-60), 10 were have TNBC present and 40 were not.

**Conclusion:** Frequency of TNBC in patients of Carcinoma breast is 35% in our society.

**Keywords:** Breast Cancer, TNBC, Female, Mammography.

## INTRODUCTION

Worldwide, breast cancer is the most frequently diagnosed life-threatening cancer in women and the leading cause of cancer death in women.[1]In the United States, breast cancer accounts for 29% of all cancers in women and is second only to lung cancer as a cause of cancer deaths.[2]Surgery is considered primary treatment for breast cancer. Many patients with early-stage breast cancer are cured with surgery alone.

Molecular and genetic studies demonstrated that breast cancer was a heterogeneous disease,[3] and had been proposed to be classified into subgroups according to different immune histochemical biomarkers.[4,5] Of which estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 (HER2) were the most important biomarkers. In the 2007 St. Gallen Consensus Meeting made a decision about adjuvant therapies (chemotherapy, endocrine therapy, and trastuzumab), operable primary breast cancers were recommended to be categorized based on the status of ER, PR, and HER2.[6]Triple negative breast cancer(TNBC) was defined as a subtype of breast cancers that were negative for ER, PR and HER2. TNBC was generally considered as the most difficult subtype to treat among these newly proposed subtypes of breast cancer because of the aggressive clinical behavior and the lack of current availability of specific targeted therapy such as selective ER modulators, aromatase inhibitors, trastuzumab, and lapatinib.[5]The metastatic potential in triple-negative breast cancer is similar to that of other breast cancer subtypes, but these tumors are associated with a shorter median time to relapse and death.

Incidence of TNBC varies and accounted for approximately 10–20% of the whole breast cancer. It has been demonstrated to affect relatively younger premenopausal women and have a different biological characteristics as well as a more aggressive disease course with higher relapse rates and frequent progression to distant metastasis. Worldwide, the incidence of breast cancer varies from 3.9/100,000 in Mozambique to as high as 101.1/100,000 in the U.S.[6,7] Geographic variation in breast cancer incidence can be attributed to racial and genetic differences, cultural differences, as well as environmental exposures that vary throughout the world.[8]

In one study aimed at assessing the breast cancer receptor status among Indian and Pakistani women diagnosed to have carcinoma breast residing in United states, it was found that Asian Indian/Pakistani women had more Estorgen Receptor & Progesterone Receptor negative breast cancer than Caucasians (30.6% vs. 21.8%, p = 0.0095).[9] In another study conducted in India 683 patients diagnosed with breast cancer were studied and 136 (19.92%) turned out to be Triple Negative breast cancer (Negative for Estrogen receptor, Progesterone receptor and her-2/neu receptor) and 529 (77.45%) had non-TN breast cancer. TN breast cancer correlated with younger age (<35 years, P = 0.003) and a higher histopathologic and nuclear grade (P< 0.001) with a higher relapse rate (14.7% for TN breast cancer and 6.6% for non-TN breast cancer).[10]In still another study, the reported frequency of triple negative receptor status was found to be present in 25% of the patients.[11]

We could not find any study conducted in Pakistan which has assessed the frequency of this aggressive subtype of breast cancer in our local population. By

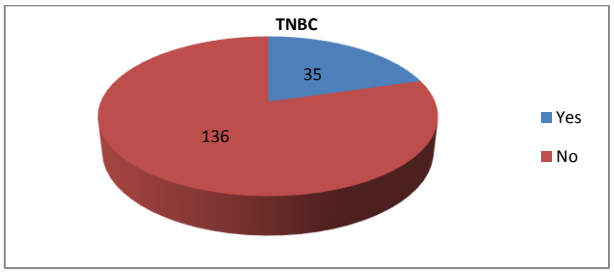
conducting this study we will be able to find out the frequency of triple negative receptor status in our local patients with breast cancer. This will not only add information to our local database but if found to be high will enable us recommend routine screening for the receptor status in breast cancer patients to find out those with triple negative status and provide these patients close monitoring and more aggressive treatment.

## METHODOLOGY

This descriptive cross-sectional survey, was conducted at Surgical Unit III, Nishtar Hospital Multan, we included 171 females between 30-60 years of age diagnosed to have breast carcinoma on histopathology whereas those unfit to undergo surgical excision, established metastatic disease were excluded from the study. Each patient was assured for maintaining privacy and confidentiality and that the name of the patient was not 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 areference laboratory(Shaukat Khanam Memorial Trust Hospital) for immune staining for presence or absence of Esterogen receptor, Progesterone receptor and Her / neu receptor. SPSS 19th version was used for data analysis. Frequency and percentages were calculated for qualitative variables like triple negativereceptor status (present/absent).

## RESULTS

Total patients included in this study were 171 (100%) all were female. These 171 patients were divided into 3 groups, patients from 30-40 years included in group 1, age 41-50 included in group 2 and patients from 51-60 years included in group 3. According to age patients in which TNBC was present were have mean age 44.06 and standard deviation 9.107 similarly patients in which TNBC was absent were have mean age of 44.32 and standard deviation 8.953. According to TNBC patients of group 1 (30-40 years), 13 were have TNBC present and 53 were not, out of 55 patients of group 2 (41-50 years), 12 were have TNBC present and 43 were not, similarly out of 50 patients in group 3 (51-60), 10 were have TNBC present and 40 were not. As regard to the age of patients out of 171 patients, out of 66 patients in group 1 were have size of tumor 2.55, 55 patients in group 2 were have size of tumor 2.56 and similarly out of 50 patients in group were have size of tumor 2.52.




## DISCUSSION

Breast cancer is a strikingly heterogeneous disease with variable clinical, pathological and molecular features.[12] It was characterized by size only for many years with significant management limitations. Later on, histological classification system was introduced which divided BC into 18 different subtypes and invasive ductal carcinoma not otherwise specified (IDC NOS) was found to be most common variety. However, this histomorphological division also failed to form homogeneous groups for treatment categorization. This heterogeneous nature of the disease has significant implications both for physicians and their patients increasingly as treatments are now targeted towards molecular markers. So gene expression profiling came into existence and five distinct gene expression profile based subtypes have been identified by cDNA microarray analysis associated with distinct treatment strategies and prognosis. Three of these are derived from ER-tumors (basal like, HER-2 neu positive and normal like) and two from ER+ subtypes (luminal a and b).[13] Still, there are certain BC subtypes that neither express steroid receptors nor over express HER-2 neu proteins the so called TNBC. This variety accounts for 10-17% of all breast cancers.

Current study focuses on frequency of TNBC in Pakistani women with context of age at presentation. Pathological record of 4715 samples was studied. TNBC was found in 815 patients. Frequency revealed is significantly closer to upper margin of the range quoted worldwide.[14] Majority of the patients had age < 50 years at presentation. Mean age of diagnosis of TNBC is 46.26 ± 12.22 years which is significantly younger than that quoted worldwide. A study conducted at Women College Hospital and University, Toronto, Canada, revealed frequency of 11.2% with mean age of presentation as 53 years. More than 90% of TNBC fall within basal like subtype (BBC) so called for its gene expression type that mimics basal epithelial cells in other parts of the body and characteristics morphology that includes high proliferation rate, central necrosis and pushing border. Basal like breast cancers are over represented in African-American women,[15] and in BRCA-I mutation carriers. After adjustment for age and stage at diagnosis, African-American women are almost 3-fold more likely than white women to have TNBC. It should be emphasized that not all TNBC are BBC and vice versa although there is a considerable overlap between them with 25% discordance rate.[16]

Although TNBC are defined by IHC analysis, currently there is no established criteria to diagnose BBC. However, immunohistological markers characterizing BBC are ck5, ck6, ck14, ck18, p63, p-cadherin, vimentin, EGF, HER-1, c-kit and IGFR TNBC constitutes a clinically challenging type as it occurs more frequently in younger women < 50years,[17] African-American women, oral contraceptive use > one year, BRCA-I mutation carriers and women in low socioeconomic group. TNBC are histologically aggressive with poor prognosis,[18] high mitotic grades, of large tumor size, more aggressive expression profile with low bcl-2 but high p53 and ki 67 expression leading to poorer OS, breast cancer specific survival (BCSS) and relapse free survival (RFS). In general, adjuvant therapeutic options for TNBC include cytotoxic agents and targeted therapies. Notably

TNBC can have higher pathological complete response (pCR) to chemotherapy especially taxanes and anthracyclines but early relapse is more likely. Targeted therapies currently being developed or under evaluation include inhibition of poly adp-ribose polymerase-1 (PARP-1),[19] epidermal growth factor receptor (EGFR) also known as HER-124 and vascular endothelial growth factor (VEGF). None of these have yet reached approval level by US FDA. Not only therapeutic options are limited for TNBC but also there are no current guidelines that specifically adhere to the management of this grave variety culminating towards a clinical dilemma both for patients as well as clinicians. TNBC is a heterogeneous disease with high recurrence and poor survival rate which poses important clinical challenge. Few studies to-date have focused on etiologic risk factors and currently little data is available in Pakistan on its true incidence and etiology. It is hoped that these results would be extended further. There is no clear proven effective single agent that targets a driving vulnerability in TNBC. This also provides a wide array for researchers and novel therapeutic options are needed to counter this aggressive tumor affecting women in their peak life.

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