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RESEARCH ARTICLE

Epidemiological Profile and Clinicopathological Correlates of Triple Negative Breast Cancer Patients at Regional Cancer Centre

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Abstract

Background: Breast Cancer is the most common cancer among woman worldwide. In India breast cancer remains the leading cause of both incidence and mortality. Triple negative breast cancer is more difficult to treat as it does not respond to hormone therapy medicines or medicines that target receptor proteins (like HER 2 Neu). It is crucial for the physician to know the status of the disease as the patient can be subjected to a whole new avenue of treatment. The present study was done to assess the epidemiological profile and clinicopathological correlates of patients of triple negative breast cancer. **Material and Methods:** This retrospective study was carried out in Acharya Tulsi Cancer and Research Institute located in the state of Rajasthan, Bikaner, India, among Ca Breast patients presenting to Medical Oncology, Radiation Oncology and Surgical Oncology outdoor & indoor from April 2016 to March 2017. Out of the total 1017 patients of carcinoma breast 957 were included in this Study. Exclusion criteria was non availability of ER, PR, HER2 neu status reports because of various reasons like affordability. Out of the total 957 patients 249 were found to be triple negative. Statistical analysis was done using IBM SPSS version 21. **Results:** Mean age of the patients was 46±11.23 years. Out of total 249 patients of triple negative breast carcinoma, 91 (%) were found to have had clinical staging I and II (Early stage) and 158 (%) patients were found to have clinical staging III & IV (Late Stage). Mean size of the tumor was 3.6±1.94cm. 151 (60.6%) were pre-menopausal, 103 (41.4%) and 12 (4.8%) patients had positive family history. All of or patients diagnosed to have Ductal type of carcinoma. Lympho-vascular invasion was seen in 51 (20.5%) patients and High grade Histological Grading was seen in High Grade 169 (67.9%) patients. 172 (69.1%) undergone MRM (Modified Radical Mastectomy) and BCS was done in 74 (29.7%) patients. After comparison of triple Negative Breast Cancer with non-triple Negative Breast Cancer, lower age, later stages (III and IV), pre-menopausal status and high grade (on histology) were significantly more in negative type of Ca breast. Occurrence of early Menarche (< 13 Years) and history of OC pills used was almost equal in both the groups. **Conclusion:** Triple Negative Breast Cancer was found to present at an earlier age and more in pre – menopausal women. Such patients presented with a higher histological grade of tumor and late stage of presentation. There was no statistically significant association between TNBC and age of menarche, use of OC pill, previous exposure to radiotherapy and positive family history in first degree relative.

Keywords: Epidemiological profile- Triple negative breast cancer- clinico-pathological characteristics

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Introduction

Breast Cancer is the most common cancer among woman worldwide and second most common cancer overall [1]. In India breast cancer remains the leading cause of both incidence and mortality. Breast cancer, accounting for 25% of all cancers [2]. It is by far the most common cancer in women, both in more and less economically developed regions with slightly more cases in less developed than in more developed regions [3]. The higher incidence of breast cancer is possibly associated with higher median population age, robust early detection programs, better control of other causes of early life mortality and recent increase in obesity. The rising

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breast cancers incidence in women of developing nations has also been attributed to "westernized" lifestyle changes including dietary changes, decreased exercise and reproductive changes such as delayed childbearing, lower parity and reduced breast feeding [4].

Triple negative breast cancer (TNBC) refers to any breast cancer which does not show expression of estrogen receptor (ER), progesterone receptor (PR) and Her2 neu. About 10 – 20 percent of the breast cancer cases are triple negative. Triple negative breast cancer is more difficult to treat as it does not respond to hormone therapy medicines or medicines that target receptor proteins (like HER 2 Neu) [5]. Triple-negative breast cancer is considered to be more aggressive and have a poorer prognosis than other types of breast cancer. It tends to be of higher grade than other types of breast cancer. TNBC represents a heterogenous subtype of breast cancer that is beginning to be refined by its molecular characteristics and clinical response to a targeted therapeutic approach. Until recently the backbone of therapy against TNBC has been cytotoxic chemotherapy [6]. However, the breast oncology community is now seeing encouraging clinical activity from molecularly targeted approaches to TNBC. This makes it crucial for the physician to know the status of the disease as the patient can be subjected to a whole new avenue of treatment [7]. The present study was done to assess the epidemiological and clinicopathological profile of patients of triple negative breast cancer and its association.

Materials and Methods

This retrospective study was carried out in Acharya Tulsi Cancer and Research Institute located in the state of Rajasthan, Bikaner, India. Study was done on Ca Breast patients presenting to Medical Oncology, Radiation Oncology and Surgical Oncology outdoor & indoor. Duration of the study was from April 2016 to March 2017. After taking clearance from Ethical Committee and consent from the eligible participants, data was collecting with the help of pre-tested case record pro-forma. All patients who were diagnosed with Carcinoma Breast and Triple negative were included in the study. Exclusion criteria was non availability of ER, PR, HER2 neu status reports because of various reasons like affordability.

Method of Diagnosis

Patients were diagnosed by FNAC and confirmed by core needle biopsy. Under local anaesthesia a core biopsy needle was used to sample breast tissue at clinically palpable site changes felt or sometimes where required done under an ultrasound guidance. ER, PR Her2 status was determined by immunohistochemistry.

Statistical analysis

Data was entered into Microsoft excel data sheet and was analyzed using IBM SPSS 22 version software. Categorical data was represented in the form of Frequencies and proportions. Chi square test, Fisher Exact tests were used as test of significance for qualitative data continuous data was represented as mean and standard deviation. p value (Probability that the result is true) of 0.05 was considered as statistically significant after assuming all the rules of statistical tests.

Out of the total 957 patients of carcinoma breast, 249 were triple negative Ca breast patients and remaining 708 were non-triple negative Ca breast patients, were taken for comparison of clinicopathological characteristics.

Results

In the present study, mean age of the patients was 46±11.23 years. Out of total 249 patients of triple negative breast carcinoma, 91 (36.5%) were found to have had clinical staging I and II (Early stage) and 158 (63.5%) patients were found to have clinical staging III & IV (Late Stage). Mean size of the tumor was 3.6±1.94 cm. 151 (60.6%) were pre-menopausal, 103 (41.4%) and 12 (4.8%) patients had positive family history. All of or patients diagnosed to have Ductal typeq of carcenoma. Lympho-vascular invasion was seen in 51 (20.5%) patients and High grade Histological Grading was seen in High Grade 169 (67.9%) patients. 172 (69.1%) undergone MRM (Modified Radical Mastectomy) and BCS was done

Table 1. Epidemiological Profile of Triple Negative Breast Cancer Patients

Epidemiological Profile	Values/ Frequencies
Mean Age (Years)	46±11.23
Mean Size of the Tumor (cm)	3.6±1.94
Clinical Staging:	
a. Early Stage (I, II)	91 (36.5%)
b. Late Stage (III, IV)	158 (63.5%)
Menstrual history:	
a. Pre-Menopausal	151 (60.6%)
b. Post Menopausal	98 (39.4%)
Menarche:	
a. < 13 Years	103 (41.4%)
b. ≥ 13 years	146 (58.6%)
Family History	
c. Positive	12 (4.8%)
d. Negative	237 (95.2%)
Tumor subtype:	
a. Ductal carcinoma	249 (100%)
Lympho-vascular invasion	
a. Absent	198 (79.5%)
b. Present	51 (20.5%)
Histological Grading:	
a. Low Grade	80 (32.1%)
b. High Grade	169 (67.9%)
Surgery	
a. MRM	172 (69.1%)
b. BCS	74 (29.7%)
c. Not Done	3 (1.2%)
Total	249 (100%)

Table 2. Association between Clinicopathological Characteristics and Triple Negative Breast Cancer (Comparison between Triple Negative and non-Triple Negative Breast Cancer)

Clinicopathological characteristics	Triple Negatives (%)	Non-Triple Negatives (%)	P Value
Age <40	107 (43)	183 (26)	<0.001
Late Stage (III, IV)	158 (63.5)	233 (32.9)	<0.001
Menarche< 13 Years	103 (41.4)	297 (41.9)	0.872
Pre-Menopausal Status	151 (60.6)	340 (48.0)	<0.001
OC Pill used	95 (38.2)	250 (35.3)	0.421
Positive Family History in First Degree Relative	12 (4.8)	38 (5.4)	0.738
High Grade	169 (67.9)	257 (36.3)	<0.001
Total	249 (100)	708	

in 74 (29.7%) patients (Table 1).

Table 2 shows that after comparison of triple Negative Breast Cancer with non-triple Negative Breast Cancer, lower age was significantly associated with triple negative type of Ca breast. On clinical assessment and clinical Staging, later stages (III and IV) were significantly more in negative type of Ca breast. Other factors like pre-menopausal status and high grade (on histology) were also more in negative type of Ca breast. Occurrence of early Menarche (< 13 Years) and history of OC pills used was almost equal in both the groups.

Discussion

Epidemiological Profile

On TNBC, fewer Indian studies have been published. TNBC contributes a large proportion of breast cancer deaths despite its small proportion among all breast cancers. In the present study, mean age of the patients was 46±11.23 years which showed similarity to (Thike et al., 2010; Rao et al., 2013) [8, 9] and variation from other studies (Dent et al., 2007; Suresh et al., 2013) [10, 11]. Our population was slightly younger than the ones described in western data [10] (median age 53 years). As compared to mean size of tumor in our study (3.6±1.94cm), Ishitha G. et al [12] found average size tumor was 4.3±2.56 cm. Higher number of patients had Positive family in study by Ishitha G. et al [12] (12%) as compared to our study (4.8%).

The most common histological subtype in our study was that of infiltrating ductal carcinoma (NOS), similar to other studies [13, 14]. Infiltrating duct carcinoma (91%) was primary histology morphology in a study by Atika Dogra et a [15]. In our study, 79.5% cases had shown lymphocytic infiltrate. Literature has shown that most TNBC cases with a dense lymphocytic infiltrate either intra-tumoral or within the vicinity of the tumor [16, 17]. In a study by Atika Dogra et al [15], presence of lymph-vascular invasion was found in 40% cases.

Present study shows out of total 249 patients of triple negative breast carcinoma, 91 (36.5%) had clinical staging I and II (Early stage) and 158 (63.5%) had clinical staging III & IV (Late Stage). Similar to our study, clinically stage IV was very common at presentation in accordance to the previous findings (Rao et al., 2013; Suresh et al., 2013; Niwińska et al., 2010) [9, 11, 18] followed by III and I. As compared to our findings show low grade in 32.1% and high grade in 67.9% patients with TNBC, Atika Dogra et al [15] revealed that a large proportion of patients with poorly differentiated high grade tumors (70%). Comparative findings were seen in a study by Ishitha G. et al [12] shows 46% cases had Grade II and 54% had Grade III tumors on histology as.

Regarding surgical interventions, in comparison to our study (MRM in 69.1% and BCS in 29.7% cases), MRM was performed in lesser number of cases in comparison with the study by Atika Dogra et al [15] (MRM in 80.6% and BCS 16.4% cases).

Comparison between Triple Negative and non-Triple Negative Breast Cancer

TNBC patients are usually less than 40 years as compared to the non TNBC[16]. Our study shows similar statistically significant association (p-value <0.001)) in age. Compared to other breast cancer subtypes, TNBC develops earlier in life, and consequently more often in pre-menopausal women [10, 19]. The average age of diagnosis for TNBC has been shown to be 5–10 years younger than patients with non-TNBC [20]. Premenopausal status varied from 70% of patients in Turkey [21], 48% in Lebanon [22] to 61% of TNBC patients in our study.

Positive family history of breast carcinoma was seen mainly in TNBC compares to non-TNBC. A positive family history was found in 10% of patients with TNBC in Lebanon compared with 1% of patients with breast cancer when all phenotypes are included [22]. 38.2% gave history of oral contraceptives (OCP) in our study as compared by 72% in Kwan et al. [23] study, 55% in Phipps et al. study [24], and 35% in the Turkish study [21].

High grade (on histology) was more frequently assocuated eith TNBC (67.9%) as compared to that with non-TNBC (36.3%). Similarly, patients with TNBC were more likely to have higher histologic tumor grade than those without TNBC [10, 25].

In conclusion, triple Negative Breast Cancer was found to present at an earlier age and more in pre – menopausal women. Such patients presented with a higher histological grade of tumor and late stage of presentation. There was no statistically significant association between TNBC and age of menarche, use of OC pill, previous exposure to radiotherapy and positive family history in first degree

relative.

Risk Involved

Nil

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