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Epidemiology of Triple Negative Breast Cancer among Cancer Breast Patients and Their Relation to Molecular and Histological Subtypes of Cancer Breast in A Tertiary Care Centre

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ABSTRACT

Background: A unique subtype of breast cancer called triple-negative breast cancer (TNBC) is distinguished by the lack of expression of the HER2 (human epidermal growth factor receptor 2), PR (progesterone receptor), along with ER (estrogen receptor). In comparison with other subtypes of breast cancer, TNBC has been linked to a worse prognosis and an aggressive clinical course. The goal of this retrospective research is to assess the incidence of TNBC among breast carcinoma patients at a tertiary care hospital, in Chennai. This research also highlights histopathological characteristics and molecular subtypes observed within the sample population.

Methodology: This retrospective analysis was conducted among carcinoma breast patients who presented to the Department of General Surgery, Chettinad Hospital and Research Institute, in the Chennai between January 2021 and January 2024, underwent histopathological testing either by TRUCUT Biopsy or surgical resection. In this study, 58 patients with breast cancer were identified of which 2 were excluded because of lack of PR, ER, HER2/neu status. Statistical analysis was conducted utilizing IBM SPSS version 22.

Results: Overall, 56 cases had been included in our research, Of the 56 patients, 19 (33.92%) were triple negative breast carcinoma. The most common histologic variant was noted to be infiltrating ductal carcinoma (IDC) of no specific type comprising a 64.28% (n=32) of all breast cancers, followed by ductal carcinoma in situ (DCIS) and papillary carcinoma each comprising 12.5% (n=7). Other variants noted included infiltrating ductal carcinoma with medullary changes (8.9%), mucinous adenocarcinoma (3%), a case of apocrine carcinoma (1.7%), and a case of tubular carcinoma (1.7%).

Conclusion: This analysis reveals a higher than average number (33.92%) of TBNC patients in a tertiary hospital, which is in line with the studies done globally. This research demonstrated the need to develop tools to accurately and quickly ascertain the molecular subtypes of breast cancer to guide effective management. Further investigation is necessary to clarify biological and epidemiological factors contributing to the high prevalence of TNBC in this setting.

Keywords: *Triple-negative breast cancer (TNBC), breast carcinoma, incidence, histopathology.*

1. INTRODUCTION

One of the most prevalent cancers in women diagnosed globally, breast cancer causes significant morbidity and mortality with an annual incidence of approximately 1,000,000 cases globally.[1] TNBC is a molecular subtype of breast cancer that is distinguished by lack of HER2, PR, along with ER expression.[2] TNBC is a diverse group of tumors that are frequently linked to aggressive behaviour, high histological grade, and poor differentiation. Its prevalence differs greatly between populations, with younger patients and members of particular ethnic groups having a higher prevalence. According to Fischer et al Intra-tumour, heterogeneity contributes to drug resistance by harbouring subpopulations of cancer cells with distinct genetic mutations that can survive treatment. These resistant subclones may possess specific somatic mutations that confer survival advantages, allowing them to proliferate despite therapy. Additionally, the dynamic nature of heterogeneity may cause to emergence of novel resistant variants in response to selective pressures from treatment, complicating effective management of the disease.[3] Bauer et al. conducted a population-based investigation on TNBC, he noted that in low socioeconomic status areas, TNBC is more frequent in younger women. These women had a lower survival rate regardless of stage, and the tumors were more aggressive and detected at a later stage.[4,5] Studies indicate that TNBC patients have a significantly higher hazard for death, with a 2-year overall survival (OS) probability lower than luminal subtypes.[6] A significant association exists between menopausal status and molecular subtypes, indicating that age and hormonal factors influence subtype distribution.[6] Despite progress in breast cancer treatment, TNBC continues to pose a clinical challenge as targeted therapies and restricted treatment alternatives beyond chemotherapy are not present. This study aims to evaluate the related histopathological findings and estimate the incidence of TNBC among patients with breast carcinoma at a tertiary-level hospital. In the study by Brian et al on new targets for TNBC, he identifies TNBC as a heterogeneous disease with distinct molecular subtypes that influence treatment response and emphasises the potential of targeted therapies, for example, PARP inhibitors for the BRCA-mutated TNBC as well as anti-androgens for androgen receptor-positive subtypes.[7]

Aim: The present study was done to assess the epidemiological profile of patients of triple negative breast cancer and its relation with different histological subtypes of breast carcinoma.

Materials and Method: This retrospective study was conducted at Chettinad Hospital and Research Institute, Chennai. From January 2021 to February 2024, 58 incident cases of female invasive breast cancer were found in the Chettinad Hospital and Research Institute registry. The patients who underwent histopathological testing either by TRUCUT Biopsy or surgical resection in Chettinad Hospital and Research Institute were considered in the study. Histologically confirmed breast carcinoma and availability of PR, ER, along with HER2 status were factors to include subjects in the study. Exclusion criteria were incomplete receptor status data. The IHC data for 96.5% of cases (n = 56) could be evaluated for PR, ER, and HER2/neu receptor status, which was a requirement for inclusion in the current investigation. This research involved 56 patients, with two cases excluded because of unavailable ER/PR status, lost to follow up. After obtaining consent from the patients whose specimens were identified and after obtaining the approval from the Intra Hospital Ethics Committee the relevant data was collected. Patient demographics, histopathological diagnosis, and receptor status (ER, PR, HER2) were extracted from pathology reports. The Allred scoring system is commonly used for evaluating ER and PR, HER2 status is assessed as per the ASCO (American Society of Clinical Oncology) as well as the CAP (College of American Pathologists) guidelines, which categorise staining patterns into negative, equivocal, and positive. The subjects had been classified into the Luminal A (ER+, PR+/-, HER2-, Ki 67 <14%), the Luminal B (ER+, PR+/-, HER2+/-, Ki 67 >14%), the HER2 enriched as well as TNBC groups. Histological subtype was also recorded and the frequency of occurrence of TNBC in each histological subtype had been also investigated. IBM SPSS 22 software was employed to analyze the data after it was entered into a Microsoft Excel data sheet. Frequencies and proportions were utilized to represent categorical data. As a percentage of the whole sample size, the incidence of TNBC was computed. Descriptive statistics have been used to summarise categorical data. Research's findings are collectively summarised. We use IBM SPSS for the statistical analysis of this study due to its ease of use for analysis of data and gives us a well put study outcome.

2. RESULTS AND DISCUSSION

Age distribution: Of all the 56 cases we studied, mean age of patients was 51.16±11.69 years which is similar to multiple studies conducted globally. It shows similarity to those examined by Kakudji et al, Thike et al, Rao et al, and Verma et al.[8-11] The youngest was aged 17 years while the eldest of the population was of 74years of age. The majority of the study population 39% was made up of the 41-50years age group (n=22), followed by 51-60years (25%, n=14), 61-70years (20%, n=11), 31-40years (9%, n=5), and 4% each for those aged ≤ 30years and > 71years of age. Figure 1 shows the graphical representation of the distribution of age among the study population. Out of total 19 patients of triple negative breast carcinoma, 9 (47.36%) were pre-menopausal, 10 (52.63%) post-menopausal. In our study not much significant difference was noted among pre and post menopausal women which might be because of small sample size and may be partially a result of a delayed diagnosis or challenging access to medical care, however, it shows more tendency towards pre-menopausal women as seen in study by Verma et al.[11]

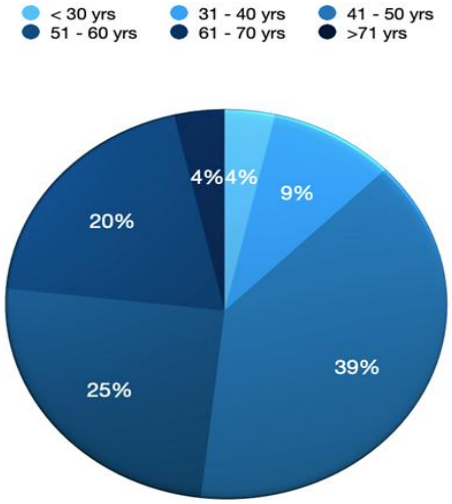

Figure 1: Age distribution of study population

Receptor status and Molecular subtype: The distribution of receptor status is summarised in Figure 2. Receptor status was noted as follows, ER+ : 53% (n=30), PR+ : 28% (n=16), HER2+ : 28% (n=16). Majority of the subjects were ER+ similar to studies reported by Kakudji et al.[8] They were categorised into Luminal A, Luminal B, HER2 enriched, as well as TNBC. TNBC accounted for 19 of 56 cases, resulting in an incidence rate of 33.92%. The distribution of TNBC cases as compared to receptor positive status is compared in figure 3. The majority of molecular subtypes (35.71%) were luminal A similar to study by Kakudji et al[8], followed by TNBC (33.92%), with the luminal B subtype (16.07%) coming in third, while only 14.28% of tumors were categorised as HER2 enriched. This is summarised in figure 4. In our study, we came across 33.92% of TNBC cases

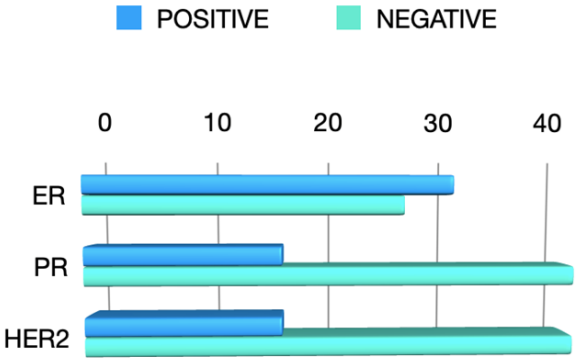

Figure 2: Chart showing the frequency of distribution of receptor status (ER, PR, and HER2).

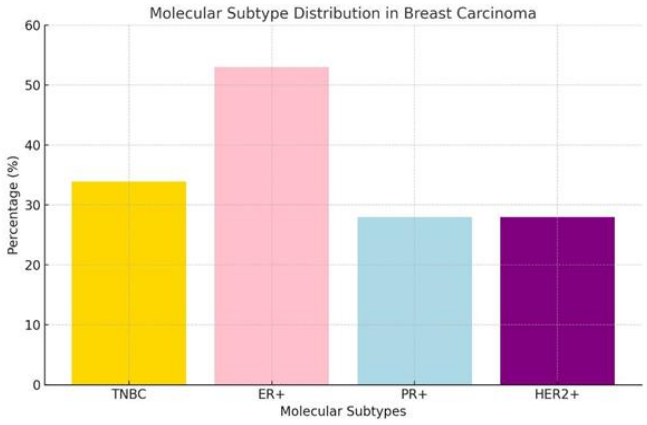

Figure 3: Molecular Subtype Distribution in Breast Carcinoma: This chart shows the percentage distribution of TNBC, ER-positive, PR-positive, and HER2-positive cases among breast carcinoma patients.

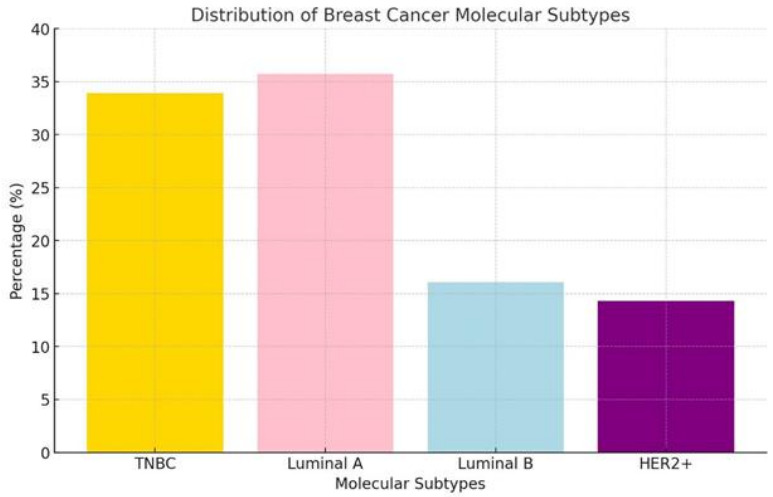

Figure 4: The chart displaying the distribution of breast cancer molecular subtypes (TNBC, Luminal A, Luminal B, and HER2+)

Histopathological subtype: The most common histopathological subtype was IDC-NST (invasive ductal carcinoma-No specific type), diagnosed in 32 patients (64.28%) similar to research executed by Kakudji et al, Rakha et al, Reis-Filho et al, Dogra et al.[8,12-14] Other histological subtypes were DCIS, Papillary carcinoma, IDC with medullary changes, Mucinous carcinoma, Apocrine carcinoma, and Tubular carcinoma each comprising 12.5% (n=7), 12.5% (n=7), 8.9% (n=5), 3% (n=2), 1.7% (n=1), and 1.7% (n=1) respectively. Among TNBC cases, the most frequency was noted among IDC-NST, 11 patients (57.9%), followed by IDC with medullary changes (4 cases, 21%), papillary carcinoma (3 cases, 15.8%), and a case of Apocrine carcinoma (5.2%). DCIS, Mucinous carcinoma and tubular carcinoma were not observed among TNBC cases. Incidence of TNBC cases among different histological subtypes has been summarised in Figure 5.

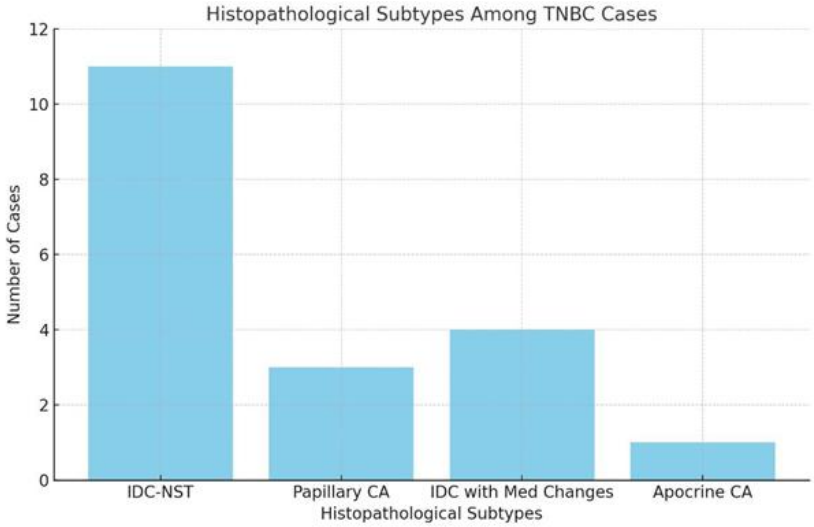

Figure 5: Histopathological Subtypes Among TNBC Cases: This chart illustrates the number of TNBC cases categorised by histopathological subtypes, including IDC-NST, Papillary Carcinoma, IDC with Medullary Changes, and Apocrine Carcinoma.

3. DISCUSSION

The findings of this study indicate that TNBC represents approximately one-third (33.92%) of all breast carcinoma cases at our tertiary-level hospital. This proportion is higher than the global average, where TNBC cause 10–20percent of breast cancers, may reflect regional and population-specific differences in breast cancer biology, and could also be due to late diagnosis of the condition.[15] Literature from regional studies mentions incidence ranging from 11.8% - 31.9%.[16-18] The observed higher prevalence of TNBC is consistent with studies from other developing regions, where TNBC is more common among younger women and associated with advanced disease at diagnosis.[15] The predominance of IDC-NST among TNBC cases aligns with established patterns in the literature.[12,19] IDC with medullary changes, a subtype with favourable prognostic

features, constituted 21% of TNBC cases, suggesting heterogeneity within the TNBC group. Other subtypes such as mucinous and tubular carcinoma were rare, consistent with their overall low frequency in breast cancer.

4. CONCLUSION

TNBC's aggressive aggressiveness and lack of targeted medicines make it a difficult clinical entity to treat. In conclusion, This three-year retrospective analysis of breast cancer cases at a tertiary care hospital brought to light the variety of histological and molecular characteristics found in the local population. The high proportion of TNBC underscores the need for early detection and tailored treatment strategies at our institution. Given the aggressive nature of TNBC and its poor prognosis, efforts to identify high-risk patients and optimise chemotherapy regimens are essential. Even though our results of incidence are in alignment with the meta-analysis by Sandhu et al[19] on prevalence of TNBC in India, recent studies show a lower overall prevalence of 25.04% by Sarkar et al[20] and a regional study at the cancer institute Chennai, shows an incidence of only 12%.[21] Therefore, patients with suspicious breast lesions should undergo TRUCUT biopsy and immunohistochemistry testing to identify the nature of the disease, and for timely management of TNBC's with chemotherapy, radiation therapy, surgery and newer treatments modality like immunotherapy, or targeted therapy (Olaparib, sacituzumab). This helps in bringing down the burden of the disease. The restricted sample size of this study may limit the extent to the findings may be applied. Larger, multicenter cohorts are required for additional investigations to validate these findings and investigate the underlying factors contributing to the high incidence of TNBC in this population.

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